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CONTENTS

SYMPOSIUM ON TREATMENT OF COMMON SKIN DISEASES

	Page
Lymphoblastoma Cutis	1
By Dr. Francis Eugene Senear	
Contact Dermatitis	13
By Dr. Edward A. Oliver	
Lupus Erythematosus	29
By Dr. Arthur W. Stillians	
Vitamins in Dermatology	47
By Dr. Michael H. Ebert	
Specific Skin Infections: Cutaneous Syphilis and Tuberculosis	65
By Dr. S. William Becker	
Pyogenic Infections of the Skin	83
By Dr. Erwin P. Zeisler	
The Treatment of Eczema-Dermatitis in Adults	97
By Dr. Herbert Rattner	
Treatment of Pruritus	109
By Dr. Maximilian E. Obermayer	
X-Ray and Radium Treatment of Diseases of the Skin	123
By Dr. Leonard F. Weber	
Toxic Dermatoses	139
By Dr. Max S. Wien	
Superficial Fungous Infections	151
By Dr. Cleveland J. White	
Cutaneous Diseases in Infants and Children	163
By Dr. Theodore Cornbleet	
Miscellaneous Skin Diseases	175
By Dr. James R. Webster	

CONTENTS

CLINICS ON OTHER SUBJECTS

	Page
Gynecologic Office Procedures	195
By Dr. Irving F. Stein	
Congenital Hemolytic Anemias	219
By Drs. Henry L. Schmitz and George J. Anday	
The Irritable Colon	227
By Dr. Frank C. Val Dez	
Common Diseases of the Respiratory Tract in Infants and Children	237
By Dr. Arthur F. Abt	
Deleterious Effects of Lipiodol and Alcohol Injections on the Tissues of the Central Nervous System	255
By Dr. A. Verbrughen	
Coarctation of the Aorta: A Presentation of Two Symptomless Patients	269
By Drs. Italo F. Volini and Gertrude M. Engbring	
Hodgkin's Disease; Vegetative and Ulcerative Endocarditis: Clinical and Pathological Conferences at Cook County Hospital	283
By Drs. Walter Schiller and LeRoy H. Sloan	
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Cumulative Index	309

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LYMPHOBLASTOMA CUTIS

FRANCIS EUGENE SENEAR, M.D., F.A.C.P.*

THE cutaneous manifestations associated with the various disorders of lymphatic origin have long been recognized as constituting an important link between the fields of general medicine and dermatology. As a rule they develop subsequent to demonstrable changes in the glandular tissues and blood picture, and here they constitute an easily accessible source of study, the clinical and histopathologic changes in the skin often furnishing evidence permitting proper identification of the nature of the underlying disorder. These eruptive changes are of even greater importance in those cases in which they constitute the first discernible signs of disease, permitting a diagnosis to be established before involvement of the glandular structures or modification of the blood picture have become demonstrable.

In the literature one finds a long list of names applied to disorders of the lymphatic system, many of them obviously synonyms, but from the dermatologic viewpoint only four of these are of any considerable importance, namely *leukemia*, *lymphogranuloma*, *mycosis fungoides*, and *lymphosarcoma*. In 1934 Keim, recognizing the tendency among an enlarging group of investigators to regard these various clinical pictures as different manifestations of the same disease process, proposed that the generic term *lymphoblastoma* be applied to

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designate the above named disorders, together with certain unusual transitional forms (Sternberg's leukosarcoma and Kaposi's lymphoderma pernicioso). This suggestion has met with rather general acceptance by the American school of dermatologists, although there are some dissenting voices.

INCIDENCE

The cutaneous changes associated with the various members of the group of lymphoblastomas are generally divided into two groups; those which show *specific* histopathologic changes in the skin lesions, and those which are regarded as *toxic manifestations*, commonly called *ids*. It has been recognized in more recent years, however, that lesions of the "id" type may contain specific cells, although clinically they are not characteristic. Generally speaking, the toxic type of lesion is much more common than the specific. Epstein and MacEachern recently reported a large series of cases in which they found in 156 cases of lymphogranulomatosis 53.2 per cent with cutaneous involvement, 7.6 per cent of these showing specific lesions and 32.7 per cent ids; in 122 cases of lymphosarcoma there were 23.7 per cent with skin lesions, 13.9 per cent being of specific type and 18.8 per cent being ids; in 90 cases of myeloid leukemia 47.7 per cent presented dermal manifestations, with 5.5 per cent of specific type and 52.2 per cent of toxic type; among 60 patients with lymphatic leukemia there were 46.6 per cent with skin lesions, of which 8.3 per cent were specific and 45 per cent nonspecific. Of four cases of monocytic leukemia, two showed specific lesions and one an id.

Various other writers have reported the incidence of cutaneous lesions of lymphoblastomatous origin and, as it is to be expected, there is considerable variation in the reported incidences. Ziegler found such manifestations in 25 per cent of his cases of Hodgkin's disease, while Cole reported cutaneous involvement in 39.3 per cent of cases of the same disorder. Pruritus, met with so commonly as a toxic manifestation in lymphogranuloma, has been reported in such variable proportions as 3.5 per cent up to 85 per cent.

SPECIFIC LESIONS

The specific lesions found in these disorders are too varied to permit of detailed description here, but in leukemia cutis and in lymphosarcoma they usually appear as nodules, plaques, or tumors.

Leukemia Cutis

According to most observers, specific manifestations occur more commonly in the skin in association with the leukemic disorders than they do in Hodgkin's disease. They are found much more frequently in cases of lymphatic and monocytic leukemia than in the more common myeloid type, where they are rarely seen.

In the typical case the leukemic *tumors* begin as small papular lesions which slowly increase in size and number. While usually slowly progressive, they may in rare instances come and go, as in the case reported by Ketron and Gay. They vary greatly in number in different cases, some showing only a few poorly defined papules or nodules, while in others they may be so numerous as to give rise to a universal eruption. Ordinarily symmetrically placed, they have a predilection for the face, especially about the eyes, and if the lesions are at all numerous they produce a characteristic leonine facies. Fully developed lesions may be nodular, flattened or discoid in shape, and may remain discrete or become confluent. The color may be bright or livid red, purplish or brownish.

One of the important types of specific changes seen in these disorders is a universal *exfoliating erythroderma*. A type commonly occurring in lymphatic leukemia is particularly significant as the skin may show the changes usually associated with Hebra's pityriasis rubra—thin branny scaling, a dark color in the skin and a suggestion of thinning or atrophy.

Mycosis Fungoides

In mycosis fungoides the specific lesions furnish the only characteristic feature of the disorder, the usual course being

a sequence of premycotic lesions which are intensely pruritic, then infiltrative, and finally tumor-like.

Lymphogranulomatosis Cutis—Ulcerative Type

In *Hodgkin's disease* the specific type of lesion is less common, but nodules, tumors and plaques may occur. One of the less common but very important varieties of cutaneous involvement in Hodgkin's disease is the ulcerative type.

In 1937 Caro and I reported a case of the ulcerative type and reviewed the findings in twenty-seven cases previously described in the literature. Since then a number of additional cases have been recorded. We stated at that time that ulceration occurred in Hodgkin's disease in three different ways. In the first variety the skin shows a number of small cutaneous or subcutaneous nodules, in some of which ulceration develops. The necrosis usually begins at the top of one of the nodules and gradually extends until it covers the surface of the nodule more or less completely. In the second type the skin is affected as the result of the extension of lymphogranulomatous changes in underlying structures. Here the involved glands become gradually inflamed, adhere to the skin, and then fistulae, leading to ulceration, form. In the third variety there develop in the skin, either as the primary manifestation of the disease, or subsequent to, but not as a direct extension of glandular involvement, large infiltrates or tumors. These break down to form extensive ulcers as a rule. The growths of this d'emblee type may precede by many weeks the other glandular or visceral manifestations of the disease.

Clinical Picture.—The ulcerative manifestations present a variety of clinical pictures. As a rule they develop and extend rapidly at the onset, but after a period of extension lasting a few weeks may remain more or less stationary for some months. In size they may vary from coin-sized lesions to ulcers the size of the palm or larger. They may be single (usually the large type), few in number or very numerous (usually the small type).

The ulcers are as a rule sharply outlined and are usually rounded or oval, but may be irregular, linear, serpiginous, or

even mangled in appearance. The borders are usually elevated but may be undermined. The bases are soft and uneven, and the floor is covered with purulent or necrotic material or granulation tissue. Free bleeding may appear when the ulcer is handled. A fetid odor is commonly apparent. As to symptoms, the patient may complain of slight pain or of severe pain of a radiating character.

Ulcerative lesions have been described as occurring in a variety of locations, but the majority of them are seen on the neck or on the upper part of the thorax.

Prognosis.—In the more extensive cases, death usually occurs in six to eight months' time as a result of progressive cachexia or following complications.

As a rule the ulcers are resistant to all methods of treatment including radiotherapy. In some instances, however, x-ray treatment causes healing, especially in those cases where the ulcerative lesion constitutes the first manifestation of the disease.

Diagnosis.—The diagnosis of such lesions is easy if they appear as a part of the general picture of lymphogranulomatosis but when they occur early in the course of the disorder are apt to be confused with ulcers due to syphilis, tuberculosis, mycosis fungoides and malignancy. Many observers have been impressed by the neoplastic aspect of the lesions. In not a few cases mycosis fungoides has been at first considered the probable cause of the lesions, and this serves to emphasize the opinion of a number of writers that mycosis fungoides and Hodgkin's disease are identical diseases. Durand, Cottentot and Mamou have recently pointed out that these two diseases may be alike in their cutaneous aspects, may present the same type of visceral invasion, the same general and hematological findings, the same evolution, and that they differ only in the histological findings. They believe that the two disorders represent closely allied pathological forms, probably of the same origin, and that they belong to the same family of reticulo-endothelioses.

The histopathologic picture of tissue from the ulcerative lesions of Hodgkin's disease is usually typical of that disorder. At times, however, the changes evoked by the inflam-

matory reaction may be so neoplastic in type that a microscopic diagnosis of sarcoma is suggested, and some authorities have maintained that sarcomatous degeneration actually takes place secondarily in such lesions.

TOXIC MANIFESTATIONS

The toxic type of eruption seen in the lymphoblastomas presents a variety of clinical pictures. Included here are pruritus, lichenoid or prurigo-like papules, pigmentations, hemorrhagic lesions, stomatitis, herpes zoster, bullous eruptions, urticaria, herpes simplex and various nondescript eruptions. Lichenification, pyodermic infections (especially furuncles) and eczematous patches may develop from the trauma induced by scratching. The *pruritus* associated with these disorders is usually severe and resistant to treatment. Pruritus as a symptom is rare in leukemia when compared with Hodgkin's disease. Roentgen therapy to the affected glands may give relief but this is usually only temporary.

PROGNOSIS

As to prognosis, it may be said that the appearance of specific cutaneous lesions in the leukemic group usually presages an early end, while in mycosis fungoides and lymphogranuloma the patient may survive for some years.

CASE PRESENTATIONS

Case 1. Leukemia Cutis

The patient, Mr. J. C., aged fifty-two years, stated that for several years he had been developing nodules in various parts of the body. These had developed gradually and were tender upon pressure but not spontaneously painful. A diagnosis of lymphatic leukemia had been made by a physician whom he had seen about two years before his entry to the hospital but it was impossible to obtain any information from this source. At the time of examination he had developed in addition to the nodules a generalized eruption which had been present for about one month. The entire cutaneous surface was affected, there being a moderate universal redness with a profuse, dry, fragmented type of exfoliation. In places, notably about the sides of the neck, about the axillae, over the arms, and in the inguinal regions, there were dis-

crete, dusky red, infiltrated plaques and nodules, the lesions varying in size from 0.5 to 3 cm. in diameter.

Hematological study showed: Hemoglobin 8.25 gm., erythrocytes 3,240,000, leukocytes 38,000, hematocrit (R) 26 per cent, hematocrit (W) 2.5 per cent, sedimentation rate 65 mm. per hour. *Differential blood smear*: polynuclears 38 per cent, lymphocytes 58 per cent, monocytes none, eosinophils 3 per cent, basophils 1 per cent. *Sternal marrow aspiration* was performed and the following findings were reported: fat (yellow) 1 per cent, fat (red) 2 per cent, plasma 66.5 per cent, "myeloid" 7.0, "red" cells 22.5, active myelopoiesis and erythropoiesis with myeloid cells in metamyelocyte-megalocyte stage and red cells mostly in normoblastic stage. Megakaryocytes were numerous and actively phagocytic. There were a few lymphocytes but no plasma cells. There was slight anisocytosis and a considerable degree of acromia. The hematologic picture was reported as that of a chronic lymphatic leukemia with almost no bone marrow involvement.

One of the enlarged glands was removed from the right axillary region and the report stated that the microscopic picture was that of a lymphoma which was differentiated by the blood picture. The microscopic evidence suggested leukemia rather than lymphosarcoma and in view of the blood findings a diagnosis of aleukemic leukemia was suggested.

The patient complained of intense pruritus and of progressive weakness. He was under observation for a period of about nine months during which time his leukocyte count varied from 17,000 to 48,000. Inasmuch as he had received a considerable amount of x-ray treatment together with prolonged arsenical therapy before entering the hospital, he was treated in the Department of Hematology with liver therapy. During the period of observation he showed no further decline in his general health and even regained some strength. The pruritus, however, continued unabated except for temporary control by means of topical applications.

Case II. Mycosis Fungoides

Mrs. W. F., aged fifty years, was first seen on November 11, 1936. She stated that several years before she had noticed a rather extensive eruption consisting of dry, erythematous and scaling patches which gave rise to intense pruritus. After these had been

present for several years she noticed that some of the patches were becoming elevated and that in some of them distinct tumors were forming.

At the time of the first examination, the patient presented a typical picture of mycosis fungoides, with lesions of all three stages of the disease present. She showed a few irregularly outlined or at times annular or crescentic patches of eczematous aspect. The vast majority of the lesions consisted of raised, infiltrated, sharply defined, bright to dark red plaques varying in size from 1 cm. to plaques as large as the palm. These plaques covered the major portion of the trunk and a number of similar lesions were present upon the extremities. In addition she showed a few scattered circumscribed projecting tumors of about walnut size. A biopsy was performed and microscopic report confirmed the clinical diagnosis of mycosis fungoides.

The patient was given x-ray treatments and after five fractional doses showed a rapid improvement. She then disappeared from observation and did not return for six months. During this interval the condition had shown considerable extension, the plaques being larger and more numerous and the number of the tumors had likewise increased considerably. The patient remained under observation more or less steadily for a period of four years. During that time she received x-ray therapy together with a large number of injections of chaulmoogra oil. With the use of this combined therapy she was rendered practically free of lesions on several occasions but, as is characteristic of this condition, the lesions soon returned and with each return became increasingly resistant to the effects of x-ray treatment.

In August of 1940 the condition was so extensive that the patient found it impossible to report for further treatment and consequently was cared for at home by her family physician. During the period of six months which elapsed before she succumbed, the patient had three attacks of peculiar character in each of which the cutaneous involvement suddenly became more intense, and the itching, which had been but little troublesome for some time, became almost unbearable, and the patient developed an extensive edema. However, after a few days of this type of reaction, the cutaneous

lesions began to involute, the itching ceased, and the edema disappeared. At the end of each of these episodes, the skin was practically free of lesions. The patient died in March, 1941, during one of these episodes and at the time of death the skin was practically free of lesions except for a few plaques which persisted over the back, thighs, and scalp.

Case III. Hodgkin's Disease with Pseudoleukemid

Mrs. M. B., aged fifty years, at the time of entrance to the Hospital stated that she had been in good health until a few months earlier when she noticed a swelling which had developed above and to the left of the suprasternal notch. This had increased rapidly in size. At about the same time she developed some redness and intense itching in the skin over various parts of the body, this being most intense over the anterior and lateral aspects of the upper extremities. Above the suprasternal notch on the left side of the neck there was found a firm nodular mass, freely movable beneath the overlying skin. The mass measured 10 cm. in width and presented well defined margins. On the right side of the neck there was a small pea-sized subcutaneous nodule present. The skin presented a generalized eruption of miliary lichenoid papules, some of them covered with blood crusts.

Examination of material taken from the mass in the neck showed a typical pathologic picture of Hodgkin's disease. Examination of blood revealed the following findings: hemoglobin 75 per cent, red blood cells 4,100,000, white blood cells 8100, lymphocytes 17 per cent, mononuclears 8 per cent, neutrophils 75 per cent.

The clinical picture was typical of a lichenoid type of id associated with Hodgkin's disease. The pruritus was intense and until x-ray therapy had begun to cause an involution of the enlarged glands, it was impossible to control this. As soon as the therapeutic effect of the x-rays was apparent, however, the pruritus subsided in large part, only to return at a later date.

This patient, who entered the hospital eighteen months ago, is still under treatment and has responded to x-ray therapy insofar as control of the involved glands is concerned. The pseudoleukemic eruption has varied in intensity

from time to time both with regard to the lichenoid eruption and the pruritus, and in general the course of these manifestations has paralleled that of the glandular involvement.

Case IV. Lymphogranulomatosis Cutis—Ulcerative Type

This patient, Miss M. S., aged twenty-three, was admitted to the hospital on July 19, 1938, at which time she presented a firm mass of supraclavicular glands on the left side of the neck. The patient stated that she had begun to lose weight in 1937 and then noticed a nodule in the left supraclavicular region. This was removed surgically and microscopic examination of the material showed the enlarged gland to be a manifestation of lymphogranuloma. In February, 1938, she was referred as a private patient to a radiologist who gave her x-ray treatment.

When she entered the hospital she showed, in addition to the enlargement of the nodes in the left supraclavicular region, some nodules in the left side of the neck and in the axillae. X-ray examination of the chest showed involvement of the mediastinal glands as well.

The patient received x-ray treatment over a period of five months and at the end of this time the nodules were no longer palpable and fluoroscopy revealed no evidence of mediastinal involvement. Three months later, however, the nodes in the region of the neck were again palpable and fluoroscopy showed parenchymal infiltration in the upper portion of the left lung with the presence of fluid in the left costophrenic sinus. The patient complained of dyspnea and orthopnea. X-ray examination showed extension of the mediastinal involvement with the presence of fluid in the right pleural cavity. Again the patient responded well to radiation over the affected areas. Some ten months later, however, the patient again complained of coughing and loss of weight, and x-ray examination revealed the presence of extensive mediastinal involvement with the presence of fluid in both pleural cavities. At this time the nodules in the left axillary region were enlarging rapidly and the overlying skin was red and inflamed. Two months later the skin overlying these glands had broken down, giving rise to a typical picture of

ulcerative form of Hodgkin's disease of the skin. Further x-ray treatment resulted in involution of the ulcerative lesion.

The patient returned some three months later because of the presence of an ulcerative lesion on the left side of the neck. At this time she presented an irregular ulceration of linear configuration from which there was a slight amount of drainage. This ulceration had developed in a location where there had been for some time an infiltration of the skin overlying the enlarged cervical glands. The clinical picture at this time was one which would unquestionably, in the absence of previous history of Hodgkin's disease, have given rise to a diagnosis of scrofuloderma. In view of the previous findings, however, it was felt that the lesion in the neck probably represented an ulcerative type of Hodgkin's disease and a study of tissue taken from the edges of the ulcer showed a typical picture of that disorder.

The patient is still under observation and at present the ulcerative lesion of the neck is showing considerable improvement.

Case V. Lymphogranulomatosis Cutis—Ulcerative Type

The patient, Miss E. L., aged fifty-seven years, was admitted to the hospital on February 2, 1940. She stated that she had felt well until November, 1939, at which time she observed a swelling in the right axilla. About one month later she complained of anorexia and noticed that she was losing weight and that she was becoming weak. At the time of entrance to the hospital, the patient presented considerable enlargement of the submaxillary glands and of the anterior and posterior cervical glands on the right side of the neck. In addition there was a large palpable gland of walnut size, painful to the touch, located in the right supraclavicular area. In the right axillary region she presented a large vegetating mass about the size of a tomato. This was of a bright red color and showed a considerable amount of necrosis and ulceration. There was a tenacious yellowish discharge. Just below this lesion on the thoracic wall there was a small ulcer about 3 cm. in width. A biopsy of one of the involved glands was performed and the microscopical report showed a typical picture of Hodgkin's disease. Material taken from the skin at the edge of

the large, vegetating, ulcerative mass showed an exactly comparable picture.

The patient received intensive x-ray therapy and, while there was some improvement in the involved glands as well as rapid healing of the ulcerative lesion, the patient pursued a rapid downhill course and death took place six weeks after admission to the hospital.

CONTACT DERMATITIS

EDWARD A. OLIVER, M.D.*

DERMATITIS venenata or eczematous dermatitis is an inflammation of the skin due to occasional, continuous, or intermittent contact with a cutaneous irritant. These irritants consist of a wide variety of substances, among the most common of which are plants, chemicals, dyes, soaps, drugs and various substances encountered in the home or in industry.

The dermatitis may be acute or chronic, and is characterized, if acute, by redness, edema and the formation of papules and vesicles. It may produce simple scaling or desquamation or it may progress to oozing, weeping and crust formation. Pruritus is nearly always a distressing symptom and the ensuing scratching often leads to secondary pus infection. In other cases due to continuous exposure, a simple dermatitis will become chronic, infiltrated and lichenified. Clinically we may find any one or a combination of these lesions present.

ETIOLOGY

This type of dermatitis may be caused by any number of irritants. The concentration of the irritant, the length of contact, and the conditions under which the exposure occurs, differentiate two types of dermatitis venenata, *nonsensitization*, and *sensitization* dermatitis (Downing).

Nonsensitization dermatitis is caused by an irritant that in given concentrations and under given surrounding factors affects nearly all human skins. An example of such an irritant is a powerful chemical applied deliberately or accidentally to the skin.

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Sensitization dermatitis, known as contact eczema or allergic dermatitis, on the other hand is a dermatitis due to repeated exposures to substances normally innocuous. The initial exposure may produce no visible irritation but subsequent exposures may produce a dermatitis at the local site or a generalized reaction. Among the common causes of sensitization dermatitis are plants, such as the primrose, chrysanthemum, tulip, daffodil, narcissus, the rhus family of poison ivy, poison oak, sumach, and the ragweed group. Other common irritants are hair dyes, clothing dyes, depilatories, nail polishes, cosmetics, adhesive plaster, dress shields, novocain and soap.

Patients with thin, sensitive skins are especially predisposed to contact dermatitis. In some individuals an allergic change is responsible for this *predisposition*. There is a distinct susceptibility on the part of some people to irritation while in others this predisposition is due to scratching, friction, sweating, maceration and traumatism of the affected parts. While in the beginning a patient may be sensitive to only one specific allergen or irritant, this sensitivity may in some cases be followed by a sensitivity to many substances, a so-called *polysensitivity*.

DIAGNOSIS

In making a diagnosis one must take a careful, detailed *history*, noting especially the patient's occupation, his habits, and the location of the eruption. When obtaining a history of exposure, one must note the time that has elapsed since the last exposure because the resulting eruption generally develops from twelve hours to several days after exposure. In the case of rhus poisoning, however, the incubation period may be even longer.

In acute cases the sudden onset and the severity of the symptoms often make the diagnosis easy. Such conditions as rhus dermatitis or dermatitis due to hair dyes are not difficult to diagnose. In cases where the disease has persisted for a long time the discovery of the offending allergen is more of a problem. When a chronic condition flares up, as it does occasionally, the etiologic agent may be discovered by ques-

tioning the patient carefully as to what he was doing at that particular time.

Inasmuch as the eczematous reaction is due to external irritation, the exposed areas are the most frequent sites for the development of the dermatitis. For example, in dermatitis due to nail polish, hair dyes, hair tonics, or face powders, the eyelids and sides of the face and neck are the locations affected; in occupational dermatitis, the dorsa of the fingers and hands; in dress dye and dress shield dermatitis, the axillae; in poison ivy, the legs, hands, forearms and genitalia; in hat-band dermatitis, the forehead; in dermatitis due to white gold spectacles, the areas behind the ears. Chronic dermatitis on the hands of housewives should point to laundry soap as the allergenic agent, but in most cases the etiologic irritant will be discovered only by careful detective work, following up every conceivable clue.

In many cases the definite localization of the eruption, the history of a sudden onset, and careful questioning will bring out a clear-cut history of exposure to an allergenic irritant.

DIFFERENTIAL DIAGNOSIS

Contact dermatitis must, of course, be differentiated from *atopic dermatitis* and *seborrheic dermatitis*.

In *atopic dermatitis* there is often obtainable a family history of eczema, hay fever, asthma, migraine headache, and vasomotor rhinitis. The disease begins as an infantile eczema, disappears or may remain constantly with the patient until at eight to sixteen years of age lichenified areas of dermatitis are found about the face, sides of the neck, in the cubital fossae and popliteal spaces. The skin generally is dry, intensely pruritic; eosinophilia is present; there is often accompanying asthma and hay fever and this condition persists into adult life.

In *seborrheic dermatitis*, there is often a history of infantile eczema, an abnormally high incidence of a male type of baldness, of dandruff, of dermatitis behind the ears, and about the nose and chest, and the skin is generally oily and greasy. The dermatitis may be diffuse or sharply circumscribed, and is made up of areas of scaling dermatitis with little or no itch-

ing. The scales are usually greasy, and the favorite sites of this disease are the scalp, forehead, angles of the nose, over the sternum, in the axillae, and in the pubic region. These two conditions should be easily differentiated from contact dermatitis.

ILLUSTRATIVE CASES

Case I. Dermatitis Due to Chrysanthemum Sensitivity

A white woman, aged fifty, came to the office October 14, 1940, complaining of an erythematous, pruritic dermatitis on both eyelids and the sides of her face and neck. This condition had been present off and on all summer but was especially worse on Sunday and Monday. Inquiry revealed that every week end she went to her country home in Michigan and while there worked in her garden. On Monday she returned to the city. Being an intelligent patient, she realized that during the week end she came in contact with some irritant and, after considerable questioning, it was discovered that she was raising a new kind of chrysanthemum, one that she had never grown before. She was asked to bring a flower in with her on the occasion of her next visit, and a patch test was done with the petals of the plant. This resulted in a positive test. She discontinued handling this particular flower and, with the application of a soothing lotion, her dermatitis quickly cleared up.

This case emphasizes the necessity of listening to the patient's story and the taking of a careful history in every case of suspected contact dermatitis, for only in this way can one arrive at a correct diagnosis. The patch test here was also a very helpful aid.

Case II. Nail Polish Dermatitis

A white woman, aged thirty-five, complained of patches of dry, scaling dermatitis on the face and neck. These patches were irregular in shape, some the size of a quarter, other the size of a half-dollar. They were flesh-colored, dry, and covered with a dry furfuraceous scale. Patches were present on each side of the neck, on the cheeks, and on both upper eyelids. There was marked pruritus, and with the skin eruption a rather marked seborrheic dermatitis of the scalp. A diagnosis of seborrheic dermatitis was made and the patient was given a mild antiseptic ointment to use

on the skin, and a stimulating scalp lotion. She improved considerably at first but the improvement was only temporary. She would apparently be free of symptoms for a week at a time, only to have the eruption recur. On the occasion of her fourth visit, it was noticed that she wore a brilliant nail polish. She was questioned carefully about this and it was ascertained that her worst attacks, as she looked back, seemed to coincide with the few days after she had applied the nail polish. She was told to discontinue using it. She did so for a month and at the end of that time reported that she had been entirely free of all symptoms. There has been no recurrence.

In cases of dermatitis of the eyelids, and the sides of the neck, nail polish should always be suspected. Dermatitis due to nail polish is quite common. The picture is always characteristic; the fingers and hands are not involved, but the common locations are the eyelids, the sides of the neck and chin, and occasionally areas on the trunk. The allergen may be the dye, the solvent, or the perfume in the polish.

Case III. Dress Shield Dermatitis

A white woman, aged forty, was first seen on January 29, 1941. She stated that she first noticed a pruritic dermatitis in both axillae about January 7. There was considerable itching and burning, especially after wearing a new rubber-covered dress shield, but she was able to control these symptoms by the constant application of a soothing lotion. She went to Florida on a vacation and while there the pruritus and dermatitis became so annoying that she consulted a physician who prescribed butesin picrate ointment for local use. This aggravated the condition so badly that at the suggestion of her husband she applied a strong Whitfield ointment. When she appeared at the office on January 29, she had a severe, painful, and pruritic vesicobullous dermatitis in both axillae and extending down to the inner aspects of both upper arms. A solution of aluminum subacetate was prescribed for local applications and she was directed to use 1 ounce of this solution to a pint of cool water as wet compresses. Four days later she was so much improved that a soothing ointment of equal parts of Lassar's paste and cold cream was prescribed. Within a few days she was entirely well. She was advised to get new dress shields and to wash them in an alkaline solution before wearing them.

This case serves to illustrate several important items. A careful history taking would have revealed that the dermatitis in her axillae was a contact dermatitis due to dress shields, a depilatory, or a new dress. Strong ointments, such as Whitfield's and butesin picrate, should not have been used on an acutely inflamed surface. Nature should have been given a chance and the inflamed areas treated with soothing lotions and wet compresses of solutions, such as dilute aluminum subacetate.

Dress shield dermatitis and dermatitis from the wearing of other rubber goods, such as sanitary belts, is quite common. A dermatitis in the axillae should always call for a careful inquiry into the wearing of new dyed dresses or waists, the use of deodorants, or the wearing of new dress shields. Inasmuch as dress shields are a necessary part of a woman's wearing apparel, it is well to know that this type of dermatitis can be prevented by having new dress shields washed, before wearing, in an alkaline solution of soap and soda ash, or soap and ammonia (Schwartz).

Case IV. Primrose and Christmas Tree Dermatitis

A white woman, seen first on December 31, 1937, suffered from a severe vesicobullous dermatitis confined to the right hand, the right side of the face, and the neck. The hand was badly swollen, a large bulla occupied the center of the palm, and on the sides of the fingers were numerous tense small vesicles. She was questioned carefully regarding possible contacts and it was learned in the course of this questioning that on Christmas she had received a large primrose plant which she had tended carefully all week, removing dead leaves and watering it daily. She had also decorated and handled the Christmas tree. Naturally the primrose was suspected of being the irritant and she was advised to get rid of it. She was given a soothing lotion similar to a calamine lotion for local application, and wet dressings of aluminum subacetate solution, diluted 1 ounce to the pint of cool water. Within a week she had entirely recovered.

On December 30, 1938, she again reported to the office with a similar attack, just as severe as the one she had the year before. This time there was no history of contact with primroses but she had again decorated the Christmas tree and been in contact with it all week. The same treatment caused an immediate cessation of

symptoms. What was at first thought to be a primrose dermatitis was actually an evergreen dermatitis.

Among the causes of contact dermatitis, first place should probably be given to certain flowers, woods and weeds, and one of the commonest irritants encountered in the plant family is the primrose. It is quite common to see a number of cases of primrose dermatitis at Easter time, and in cases of contact dermatitis involving the hands and face of elderly ladies, one should always think first of primroses.

Case V. Polysensitivity

A dentist, aged thirty-five, was first seen on February 9, 1926, with an irritant dermatitis of the fingers, thumbs and dorsal aspects of both hands. This condition had been present for the past six years, disappearing at times only to recur when he used novocain and butesin to extract and fill teeth. At times he developed an irritant dermatitis on the penis and scrotum. The skin of the fingers and thumbs of both hands was dry, infiltrated, scaling and the finger tips were fissured and painful. He knew that he was sensitive to novocain and butesin but felt that, to continue practicing his profession, he had to use them. He took measures to protect himself by wearing rubber gloves and using novocain only when it was absolutely necessary, and under the use of soothing ointments and radiotherapy, the skin improved a great deal.

He was not seen again until November 2, 1928, when he returned with a recurrence of his eczema. In addition to the painful dermatitis involving his fingers, there was an erythematous, pruritic dermatitis on his upper lip and on the sides of his nose. Under treatment, and abstention from novocain, the eruption again cleared up.

On January 3, 1930, he was seen again. He stated that he had been well for a long time though his fingers were dry, crusted and fissured. He now had a severe irritant dermatitis on the right side of his face. His right eyelid was swollen and edematous and the skin of the right side of his face was swollen, erythematous and pruritic. He stated that the previous evening he had played with a red painted game with his young son and very shortly afterwards he noticed an irritation on the right side of his face. He had rubbed his right eye quite forcibly and that morning awoke with a swollen and edematous eye, and a severe dermatitis

of his face, probably due to contact with the dye in the red paint, which usually is para-nitranilin red. This dermatitis refused to respond to the usual therapeutic measures and he was incapacitated for a month. The eruption subsided at the end of about five weeks, and although he may have been bothered with an acute flare-up now and then, he did not visit my office again until October, 1931, almost two years later. At that time he had another flare-up involving his fingers and hands. This attack quieted down under treatment and he remained practically free of all symptoms until February 16, 1934. I was called to his home that evening and found him confined to his bed with a swollen and edematous face, which was also the seat of a severe dermatitis. The eyelids, nose and lips were badly swollen and irritated and while the fingers were not involved, there was a pruritic, erythematous dermatitis that involved his wrists and forearms. He felt that this attack was entirely different from any previous attack he had suffered, and felt certain it was due to the fish he had eaten at a dinner the previous night. He said, then, that for the past two years he had noticed an increasing tendency for certain foods to upset him and produce dermatitis in these areas, chiefly on his lips and about his nose.

He was sent to the hospital for food tests and general observation and while there it was noted that he reacted strongly to injections of sodium thiosulfate and to dextrose as well as injections of his own blood. After several weeks in the hospital his skin and general condition improved sufficiently for him to leave and take a two months' vacation, from which he returned looking better than at any time within five years. The results of his hospital investigations were essentially negative although careful studies were made which included blood chemistry, blood and metabolism. Food and patch tests were also negative.

On January 22, 1937, three years later, he was again seen for a severe attack involving his face, the backs of his hands, and wrists. He blamed this attack on contact with the fur coats of his women patients. This attack responded quite promptly to treatment, but he was again seen, for the last time, on May 26, 1939, with a marked reaction on his chin and forearms for which he could ascribe no cause. I feel certain that, although he protected his hands carefully with rubber gloves, the condition was due to the use of novocain.

This case is one that illustrates polysensitivity. Here was a patient with a thin, blonde, sensitive type of skin, one that

was easily irritated by soap and water, wind and sun, that was first made sensitive by contact with novocain and butesin, finally developing a hypersensitivity to furs, to red paint, to various foods, to certain drugs, even to his own blood; a typical case of acquired polysensitivity.

INDUSTRIAL DERMATITIS

The National Committee of Industrial Dermatoses has agreed on the following definition of industrial dermatitis. "An occupational dermatosis is a pathological condition of the skin for which occupational exposure can be shown to be a major causal or contributory factor."

Dr. C. Guy Lane believes that seven items are of importance in the history of an industrial dermatitis.

1. That the time relation between the exposure to the agent and the onset of the dermatosis is correct for that particular disease.
2. That the individual has an occupation with a high cutaneous morbidity.
3. That he has been working in contact with an agent known to have produced similar changes in the skin.
4. That the site of onset of the skin disease coincides with the site of maximum exposure or trauma.
5. That some of his fellow workers with the same agent have similar manifestations.
6. That no possible exposure outside his occupation has been found to be an agent which could cause similar lesions.
7. That if the diagnosis is dermatitis, the history of multiple attacks, coming after exposure and re-exposure to an agent, followed by improvement and clearing after cessation of exposure, constitutes most convincing evidence that the occupational factor is a cause.

Industrial dermatitis accounts for a large proportion of the compensable disabilities in occupations today, according to Louis Schwartz of the United States Public Health Service. He believes it is a conservative estimate to say that 1 per cent of the industrial workers in the United States are annually affected with industrial dermatitis, and that the continual

introduction of new chemicals and new processes may be expected to cause an increase in this percentage.

A tabulation as to industry and cause of 6000 compensated cases of industrial dermatoses reported to the United States Public Health Service shows that most of the cases occur, in the order named, among workers in metals and machinery, domestic workers, and handlers of food.

Etiology

The principal actual causes as recorded by the United States Public Health Service are:

- | | |
|-----------------------------------------------|-----------------------------|
| 1. Petroleum oil and greases | 6. Dyes |
| 2. Alkalies, including cement
and concrete | 7. Plants |
| 3. Solvents | 8. Rubber and its compounds |
| 4. Chromic acid and salts | 9. Paints and varnishes |
| 5. Metals and metal plating | 10. Synthetic resins |

Schwartz estimates the annual loss in dollars and cents to industry from occupational dermatoses to be approximately four million dollars. A study of the compensation records of the several states shows the average loss of time per year in compensated cases is ten weeks. The average compensation paid is about \$100. The average cost of medical care per case is \$90. Industrial dermatitis, then, is of paramount interest both to employer, employee and dermatologist.

Are certain individuals more predisposed to industrial dermatitis than others?

The Negro is less susceptible to the action of skin irritants than the white man. Many employers will employ only Negroes where the occupation entails exposure to irritating dusts and dyes. Men with thin blonde skins are more easily irritated than those with thick oily skins. This is especially seen in those who work with soaps, turpentine and fat solvents. Men with hairy skins are apt to develop furuncles, acne and folliculitis when working in oil refineries, machine shops and garages.

Various portions of the skin of the same individual vary in their susceptibility to irritation. The inner aspects of the

forearms and the anterior portions of the body are much more easily irritated than are other parts.

Young people are more readily irritated than are older ones. The skin of women is much more sensitive to external irritants because of its dryness.

There is more industrial dermatitis in warm weather than in cold because less clothing is worn and there is closer contact with irritants. Then, too, perspiration is a factor. Workers who perspire excessively are more likely to develop dermatitis from solid substances such as calcium oxide, which in the presence of moisture becomes calcium hydroxide or slaked lime.

Diet, too, may be a factor in that it influences the hydrogen ion concentration of the perspiration.

Diagnosis

The problem of finding the causal agent in industrial dermatitis and determining whether the dermatitis is of industrial origin, is in some cases very difficult. Inasmuch as industrial dermatitis is contact dermatitis, the picture is in no ways different from any other type of contact dermatitis.

In the great majority of cases seen in the office and at the clinic, an accurate diagnosis can be arrived at by carefully examining and questioning the patient and by a careful consideration of those criteria mentioned on page 21. In most cases these simple measures will enable one to make a diagnosis. There are, however, many typical cases in which so many irritants are suspected and so few real clues are present that it becomes necessary to resort to patch testing. Patch testing, however, is of little value in the chronic lichenified types.

The Patch Test

Technic.—The technic of the patch test is as follows: A small piece of the suspected material is applied, or a piece of undyed linen is soaked in the solution or, if powder is tested, a small piece of moistened linen is dipped in the powder or other material. This patch is placed on the unbroken skin,

covered with a large piece of gutta percha or oiled skin, then these two patches are covered with adhesive plaster. A suitable place generally for patch testing is the patient's back. As many as thirty such tests can be made at one time. On removal of the patches at the end of twenty-four to forty-eight hours, the sites are cleansed and any reactions observed. If a reaction occurs to any given substance used in the tests, provided that substance is not a primary irritant, then one can conclude that the skin is hypersensitive to this substance. It does not prove, however, that this substance is the cause of the existing dermatitis, unless there is a history of exposure to this substance and the reaction that develops has the characteristics of the dermatitis that is being investigated. With these conditions fulfilled we have a right, then, to suspect that substance.

Evaluation of Reactions.—Sulzberger says "that the demonstration of this specific allergic hypersensitivity by means of the patch test may suggest, but does not necessarily prove, that the allergen was the cause of the presenting clinical dermatitis. For this reason the physician evaluating reactions should constantly bear in mind that a positive allergic response to a correctly performed patch test cannot possibly prove causal relationship, but can only demonstrate that there is an eczematous hypersensitivity of the particular skin site, at the particular time, and to the particular substance in the particular manner and concentration applied; vice versa, an absence of reaction to patch tests performed *lege artis* demonstrates only that the particular skin site is *not* hypersensitive to the particular substance at the particular time and in the particular manner of exposure. The absence of reaction may suggest, but does not necessarily prove, that the allergen applied was not the cause of the presenting dermatitis."

While it is generally admitted that patch tests when made properly are the most innocuous of all forms of skin tests, yet states Sulzberger, "There are grave consequences which may follow the improper or careless use of patch tests and even the greatest care and conscientiousness are sometimes unable to prevent certain ill effects." It is therefore obvious that all who perform them must be conversant with their handling

and furthermore these tests should not be performed unless definitely indicated.

Finally, in many cases of industrial dermatitis, even after painstaking investigation and careful study including patch testing, the question of whether the condition present is due to industrial exposure remains unanswered. The honest physician, then, has no alternative but to say, "I am not able to say whether or not the employee's occupation is the major factor in the production of this dermatitis."

Illustrative Cases

The following cases illustrate a few of the common industrial dermatoses encountered in office practice:

Case II. Dermatitis from Contact with Varnish Remover

M. A., a white man, aged thirty-eight, was employed in a large concern which manufactured telephones and telephone equipment. This patient's hands were swollen, inflamed and edematous while the skin of the terminal phalanges was dry, infiltrated, fissured and quite painful. The patient stated that two years before he had had a similar condition and after a short vacation and a change of work, the skin cleared up promptly. Owing to a shortage of men he was again returned to his old department where he used a varnish remover constantly. Almost immediately he developed a recurrence of his previous trouble. He attributed the condition to contact with the varnish remover and he was probably correct. He was given another rest and later transferred to other work. Under soothing ointment his dermatitis disappeared.

We know that varnish and paint solvents, the principal ones of which are turpentine, benzine, pentane, coal tar, naphtha and toluol, are often systemic poisons as well as cutaneous irritants.

Case VII. Chrome Dermatitis

A white male, aged twenty-four, was referred to me for a severe, crusted, fissured dermatitis involving the tips of the first three fingers of the right hand, the third and fourth fingers of the left hand. The skin of all the involved areas was dry, infiltrated, stiff and fissured. He developed blueprints and his occupation

necessitated immersing the affected fingers in a solution of potassium bichromate. This, then, was a case of chrome dermatitis.

Among 1000 cases of industrial dermatitis, reported by the State of Ohio, there occurred sixty cases of chrome ulceration and thirty-one cases of chrome dermatitis, or about 9 per cent of all the cases of industrial dermatitis. The electroplating industry accounted for forty-nine cases of chrome ulceration and dermatitis. A dermatitis of this type is quite common in the photographic and lithographic trades.

Case VIII. Cement Dermatitis

A white male, aged thirty-three, employed in a large shingle manufacturing company, was referred because of an eczematous dermatitis on the dorsal aspects of both hands, including the fingers and the flexor aspects of the wrists. The skin of the affected areas was dry, infiltrated, scaling, and on the tips of the terminal phalanges of all the fingers there was thickening of the skin and fissuring. His work consisted of handling cement shingles and, while he customarily wore rubber gloves, the cement dust got into his gloves and irritated his skin.

The patient's work was changed because he presented such a typical picture of cement dermatitis. Soothing ointments and radiotherapy in small doses were applied to the affected skin and after several months he made a complete recovery.

We know that it is entirely possible and probable for cement to have produced this dermatitis. The patient's explanation of how the cement had irritated his skin was undoubtedly true. Cement used in the building trade consists of lime, clay and silica in varying proportions. They produce a dermatitis known as "cement itch." When cement, such as he had been handling, comes in contact with the skin, it absorbs moisture from it and after some time causes the skin to become dry, hard and thickened. Such skin is likely to crack, and fissures and ulcers result.

Case IV. Epidermophytosis of Feet Simulating Industrial Dermatitis

The patient, a white male, was referred for an eruption on the sole of the left foot. He stated that about one week before he had

stepped on a piece of hot metal. This burned right through his shoe and blisters formed which left a raw spot. He went to the plant physician who cut the burned flesh away, treated the burn for several days, and it gradually healed. About two days after he had burned his foot, he developed three large blisters on the ball of the foot and one on the undersurface of the great toe. Examination of the left foot showed on the sole, just posterior to the ball, a crescent-shaped, scaly patch which represented the site of the burn and which was nearly healed. Posterior to this area were arranged three pea-sized, deep-seated, multilocular, "boiled sago grain" type vesicles typical of eczematoid ringworm, and on the plantar surface of the left great toe was a similar lesion but its contents were milky.

These vesicles, which the patient firmly believed were due to his previous burn, were incised, their tops removed and examined in a 25 per cent solution of potassium hydroxide. The branching mycelial threads and the spores found were those typically seen in epidermophytosis of the feet.

This, then, was not an industrial accident as the patient had originally supposed but a case of epidermophytosis, and is reported here that one may be cognizant of the fact that all cases, irrespective of their history, should be painstakingly examined.

BIBLIOGRAPHY

- Sulzberger, M. B. and Finnerud, C. W.: Industrial Dermatitis, *J.A.M.A.*, *111*: 1528, 1938.
Downing, J. G.: Dermatitis, *J.A.M.A.*, *115*: 813, 1940.
Sulzberger, M. B.: Dermatologic Allergy. Charles C. Thomas, Springfield, 1940.
Schwartz, Louis and Tulipan, Louis: Occupational Diseases of the Skin. Lea & Febiger, Philadelphia, 1939.

LUPUS ERYTHEMATOSUS

ARTHUR W. STILLIANS, M.D.*

ERYTHEMATOUS lupus is a systemic disease which is usually chronic and manifested only by lesions of the skin and mucous membranes. In rare instances it is acute, with general symptoms as well as those related to the skin; this type commonly has a fatal outcome.

CLINICAL MANIFESTATIONS

The *chief forms* are:

1. Chronic discoid
2. Chronic disseminate
3. Discoid in exacerbation
4. Disseminate in exacerbation
5. Acute disseminate

Chronic Discoid Lupus Erythematosus

The discoid form (Fig. 1), by far the commonest of these, has its first manifestations in one or several round or oval, sharply defined, red macules on the face. These resist soothing applications and soon show *adherent scales* which, when removed, are seen to have peglike projections upon the under surface. In the sites from which they are taken, corresponding pits are seen. These scaly lesions become slightly elevated, enlarge and develop a zone of *telangiectasis* about the scaly portion and atrophy at the center. The central *scar* sometimes retains the aforementioned pits.

The lesions frequently merge with neighboring patches to form polycyclic figures. Occurring most often on the cheeks, they join by means of a patch on the nose to form the typical figure resembling a butterfly with open wings. Similar round

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or oval patches appear on the ears, less often on the backs of the hands and fingers and on the toes. On the scalp one frequently sees a bald atrophic spot bordered by a red zone stippled with dark brown plugs.

An ill defined patch of horny follicular plugs without scarring or erythema is sometimes seen on the tip of the nose.

These eruptions tend to be symmetrical and very rarely ulcerate. The disease is chronic, with a strong tendency to recur after being cleared up by treatment. Contrary to the statements of many authors, new lesions may occur in the



Fig. 1.—Discoid lupus erythematosus. (Dr. Harry Hedges' case)

scars. A burning sensation may be felt in the early lesions but usually there are no subjective symptoms.

The rare *telangiectatic form* is manifested by macules or slightly infiltrated nodules or nodes of a deep red to violaceous color caused by dilated superficial blood vessels which do not disappear under the diascope. No scales or keratotic plugs are seen, but the slow involution of the patch ends in central atrophy.

Rarely the early lesions of the discoid form may resemble rosacea, or may be wheals, vesicles or bullae. A comedo-like

eruption and a punctate macular one causing depressed scars have been described by several authorities.

The discoid form of the disease may begin as *chilblain lupus*, the *lupus pernio* of Hutchinson. Bluish-red macules appear on the face, ears and hands. Aggravated by cold, they at first look much like chilblains, but later become infiltrated and reveal their true discoid character.

Mucous Membrane Lesions.—The mucous membrane lesions have been well described by Kren,¹ from whom the following is taken. Upon the lips, particularly their vermilion borders, an arciform or gyrate figure may be seen spreading peripherally and clearing centrally, where the surface may be smooth with fine bluish-white lines or points. Instead the center may be eroded, covered with a yellowish pellicle, or it may already be a depressed scar. The border is elevated and covered with telangiectases extending in parallel lines toward the normal skin into which they fade. Elasticity is often lessened so that fissures occur, with bleeding and crusting. Collodion-like scales may cover the whole lesion. Upon the buccal mucosa, chiefly in the interdental spaces, are seen atrophic areas, with dilated blood vessels or bluish-white lines radiating from the center. Similar atrophic lesions may occur on the palpebral conjunctiva, on the tongue, on the cartilaginous nasal septum or the inner surface of the alae nasi.

Chronic Disseminate Lupus Erythematosus

The chronic disseminate form of the disease (Fig. 2) is manifested by an eruption of dull red macules or *plaques*, slightly infiltrated. They occur not only on the sites mentioned previously, but also on the V-shaped area of the upper chest exposed to light by the dress, the extensor surfaces of the limbs, the backs of the hands and feet, fingers and toes, the finger tips, less often on palms and soles and upon the trunk. Telangiectases may be numerous and vesicles occur frequently upon the violaceous lesions on the extremities. As may be supposed, this type is more apt to become subacute or acute than the discoid form.

With both chronic types, enlarged lymph glands, discrete and not tender, are frequently found.

Hypersensitivity in Lupus Patients.—The tendency of lupus erythematosus to produce in its victims hypersensitive-ness to light, to bacterial toxins, tuberculin, streptococcus or staphylococcus vaccines, to the shock of operation or other trauma is of great importance because of its relation to



Fig. 2.—Chronic disseminate lupus erythematosus.

recurrence and acute exacerbation. Such occurrences frequently date from exposure to sunlight or artificial ultraviolet light, to injections of tuberculin or to an operation, even of minor character.

Discoid or Disseminate Lupus Erythematosus in Exacerbation

During the course of the chronic forms the occurrence of fever, albuminuria, bone and joint pains and malaise are

warnings of an impending acute exacerbation. The lesions become edematous, brighter in color, and new ones appear. On the mucosae, bullae may form, crusting and leaving erosions, even ulcers at times, with the floor covered by gray or yellow pellicle. Hemorrhagic macules, papules and vesicles appear on the extremities and these, with the mouth lesions, often produce a strong resemblance to erythema multiforme.

The fever is low and fluctuates irregularly. Albuminuria is usually moderate, with few casts and traces of blood. Stickney,² who has made a study of it, believes that it is due to toxic irritation and that the kidneys like the skin, may return to normal during remission of the disease. A secondary anemia with leukopenia, sometimes a relative lymphocytosis or thrombocytopenia, is common. The white cell count may be only a low normal but fails to rise with elevation of the temperature. Rapid sedimentation of red cells is the rule.

The joints are frequently involved before the appearance of the skin lesions, according to Slocumb.³ Twenty per cent of patients with chronic disseminate lupus have arthritis or arthralgia. Fifty-seven per cent of those with the subacute disease and 63 per cent of those with the acute form also suffer from it. The symptoms resemble those of rheumatism, but, though salicylates relieve the pain, they do not reduce the fever.

Other serous surfaces, such as the pleura and pericardium, are commonly inflamed, and even the peritoneum may be inflamed in some instances. Endocarditis, often found at autopsy, is not easy to detect by clinical means. The lymph glands are usually enlarged, the spleen and liver not seldom. Diarrhea is the commonest gastro-intestinal symptom. Pain in the abdomen may simulate a surgical emergency and lead to an unnecessary operation.

Choroiditis and retinitis, sometimes hemorrhagic, are not infrequent in the severe cases. Maumenee⁴ reports five such cases which he considers a manifestation of the general toxemia not peculiar to the disease.

Keil⁵ considers the possibility of a relationship between erythematous lupus and dermatomyositis. He reports a case

with features of both diseases and with lead in the urine, and refers to the theory of Ludy and Corson.⁶

Rose and Pillsbury⁷ mention the relationship of Raynaud's syndrome and periarteritis nodosa as well. Raynaud's attacks or thrombocytopenic purpura may antedate the skin lesions.

Acute Disseminate Erythematous Lupus

Acute disseminate erythematous lupus is rare, although according to Ludy and Corson⁶ it is rapidly increasing in fre-



Fig. 3.—Subacute disseminate erythematous lupus.

quency. It exceeds in severity the subacute and acute exacerbations described above and differs in the fact that no history or signs of chronic lupus erythematosus precede it.

Along with or preceding the *severe systemic disturbance* and *great prostration*, a *puffy erythema* appears upon the face, involving much of it. There may for a time be a sharp demarcation about the eyes and at the frontal hair line, but the eruption soon spreads over these and involves large portions of the extremities and trunk (Fig. 3). The skin between the inflamed patches may show the *Nikolsky sign*—separation of its layers on moderate side pressure. Hemorrhagic vesicular and bullous lesions are numerous. Mucous membrane involvement causes great distress and patches of alopecia appear about the lesions on the scalp.

The course is often steadily and rapidly downward in spite of all therapeutic efforts, but remission may occur, last for months or even years; then recurrence brings the fatal issue. The fever becomes typical of sepsis, but blood cultures are commonly sterile until secondary infection occurs. Pneumonia, septicemia or pyemia usually ends the struggle.

PATHOLOGY

The histopathology of the *skin* consists of dilatation of blood and lymph vessels in the cutis with edema most marked in the papillary layer. liquefaction necrosis of the basal layer, fragmentation of the collagen and elastic fibers in the stratum just below the papillae, and a perivascular and periglandular infiltrate of lymphocytes. Hyperkeratosis, with the formation of horny plugs in the follicles, the mouths of sweat ducts and between them, is characteristic. Atrophy follows.

The significant pathology is found in the *internal organs* in the severe forms of the disease. Baehr, Klemperer and Schiffrin⁸ found microscopic alterations in the small blood vessels of the kidneys in twenty of the twenty-three cases that they studied. Similar vascular damage was found in the skin and many other organs. It ranged from simple dilatation with extravasation of serum and blood to endothelial proliferation resulting in thrombi and degenerative and necrotizing areas in the blood vessel walls, and a peculiar hyaline degeneration producing in the kidney a stiff appearance of the vessels—the “wire loop lesions.” Baehr and associates have

never seen these in human tissues except in eclampsia, but they are seen in horses which have been immunized by repeated intravenous injections of live bacteria.

These authors liken the photosensitiveness of the skin of lupus erythematosus to the *Shwartzman phenomenon*: intense vascular damage with hemorrhage and necrosis in tissues sensitized by a local injection of bacterial toxin, followed after a suitable interval by an intravenous injection of the same or a different toxin, or even of an entirely unrelated protein. These reactions are elicited more easily by mixture of testicular extract with the bacterial toxin or when pregnant animals are used.

In the fatal cases of lupus erythematosus, any or all of the *serous membranes* are involved: joints and pleura most often, pericardium frequently, sometimes the peritoneum. Verrucous endocarditis is common and not seldom is of the atypical, nonbacterial type characteristic of the Libman-Sacks syndrome. Thrombi or emboli are found in many tissues. Cloudy swelling or other disease of the liver, splenitis or perisplenitis may be present.

ETIOLOGY

The outstanding fact is the great predilection for the *female* evident even in childhood; 75 per cent of the chronic cases, 90 per cent of the disseminate and nearly all the acute cases are in females. All ages are represented, but women between puberty and the menopause are in large majority. Strange to say, there has been no definite endocrine factor discovered. Possibly it may be found by further investigation of the Shwartzman phenomenon. The influence of pregnancy, already noted, is suggestive. Pusey and Rattner⁹ report a case connected with menstruation in which adrenal gland therapy seemed to prevent recurrence of the facial eruption. Baehr² in a discussion of his paper stated that sex predominance may possibly be related to the cyclical variations in ovarian functions which influence the skin.

There is in many of the chronic cases of lupus erythematosus a close association with *tuberculosis*. This is not so evident in the acute cases, in many of which not the slightest

evidence of tuberculosis can be found. The advocates of the tuberculous theory of the causation of lupus erythematosus are under some difficulty to explain why the skin lesions of lupus erythematosus never give histological evidence of tuberculosis and how the bacillus of Koch kills without leaving its fingerprints. Goeckerman¹⁰ presents strong statistical evidence against its tuberculous nature.

Brocq's theory that toxins from *infectious foci* of various kinds are responsible has long been the favorite among dermatologists and will probably remain so until a specific cause is found.

The *porphyrins* sometimes found in the blood of light-sensitive individuals, including many with lupus erythematosus, have been suggested as an etiologic factor. The discovery of Goeckerman, Osterberg and Sheard¹¹ that they could increase the blood porphyrins in light-sensitive individuals by an exposure to ultraviolet light seems to indicate that the porphyrins are a consequence rather than a cause of photosensitivity. Similarly Ludy and Corson⁶ think that *lymphocytosis* may be a response to the action of light. These authors have reported a study of eighteen cases, in fifteen of which they found an excess of *lead* in the tissues. Among twenty controls, lead in noticeable quantity was found in only three, and then only a slight amount. They suggest that lead poisoning may be responsible for the damage to the small blood vessels. Keil,⁵ too, in his case found lead in considerable quantity.

Belore¹² suggests that, in view of the repeatedly sterile blood cultures in acute cases with every other sign of sepsis, lupus erythematosus may be another of the diseases due to an *ultramicroscopic agent*.

Baehr⁸ sums up the present idea of the etiology well when he says: "It would seem that the disease is conditioned, not by the nature or severity of the local infection, but by a peculiarity in the constitutional reaction of the host."

PROGNOSIS

The cases of *chronic discoid lupus* will with few exceptions subside under treatment, leaving scars (Fig. 4). and in all

probability will recur after months or years. A few will become acute and rapidly fatal.

The *chronic disseminate type* furnishes a much larger percentage of subacute or acute exacerbations. The prognosis in these is in relation to the measure of acuteness and the signs of internal involvement.

For the more severe of these and for the *acute exanthematous type*, little hope can be offered. The fatal outcome may be reached in a few weeks or may with careful attention be deferred for some months.

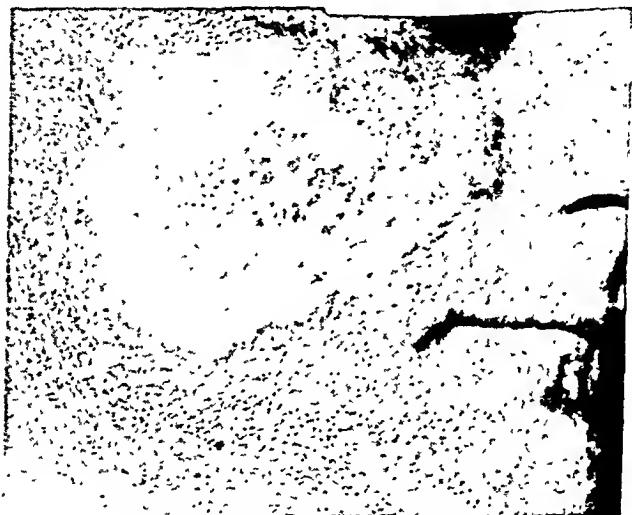


Fig. 4.—Scar caused by lupus erythematosus, with several recurrent papules within it.

The *scars* of lupus erythematosus are, like those of lupus vulgaris and burns, subject to malignant change in a small percentage of cases. The epitheliomas originating there are usually squamous celled; very rarely sarcoma begins in a scar of this kind.

DIAGNOSIS

Plaques on the face, scalp, ears or extremities showing a peripheral zone of *telangiectasis*, and next a zone covered by *adherent scales* with horny pegs on the lower surface and in the center a *scar* are diagnostic of the discoid variety of the

disease. If the lesions of this nature are arranged rather symmetrically across the nose in butterfly fashion there can be no doubt. Involvement of the lips or buccal mucosa may sometimes be diagnostic without skin lesions. A remaining discoid lesion may clarify an acute eruption otherwise difficult of diagnosis.

A low, irregular fever, *arthralgia* or *arthritis*, the pain of which is relieved by salicylates without affecting the fever, *leukopenia*, *petechial eruptions*, slight or outspoken *albuminuria*, signs of *pleural*, *pericardial* or *endocardial involvement* with persistently *negative blood cultures* should, according to the Reifenssteins¹³ and Rose and Pillsbury,⁷ justify a diagnosis of lupus erythematosus even before the typical skin signs have appeared.

DIFFERENTIAL DIAGNOSIS

Senile keratoses are covered by horny crusts showing center pegs on the lower surface, but these are not scales and there is always a history of spontaneous loosening of such crusts from time to time, then formation of a new one on the same site. They are few in number and enlarge very slowly, and have no peripheral telangiectasis or central atrophy.

Lupus vulgaris usually begins early in life, has no such predilection for the female, usually shows somewhere typical apple-jelly macules or papules, translucent yellow under the diascope and easily punctured with a fine probe. Ulceration is usually present. *Lupus vulgaris erythematoides* of Leloir lacks ulceration but has the other features typical of its group, including a strong tendency to asymmetry, frequent involvement of the trunk and avoidance of the scalp. The primary lesions of *lupus vulgaris* are small, producing a finely scalloped border, while *lupus erythematosus* patches are coarsely gyrate. The histopathology of the two diseases furnishes a sharp contrast.

Tertiary nodular syphilis is seldom symmetrical, and often develops in one direction, forming a serpiginous border usually ulcerated. The lesions are nodules. A positive serum test for syphilis is of value but a negative test does not rule out syphilis. Biopsy should be conclusive.

Rosacea, like *lupus erythematosus*, involves the flush areas of the cheeks and the nose, but also the chin and the glabella. The lesions are soft papules or papulopustules which come and go quickly, varying from one day to the next, and do not cause scars. The frog-blossom nose is large, fleshy and bright red; the nose of *lupus erythematosus* is of normal size, grayish, and covered by horny plugs.

The various forms of *Boeck's sarcoid* may resemble the deeply infiltrated form of *lupus erythematosus*. Histopathologic studies must decide.

Upon the lips *cheilitis exfoliativa* may suggest *lupus erythematosus*, but it does not show the pegs on the undersurface of the scales, only the crimson border of the lip is involved, with no polycyclic extension upon the skin, and other lesions of seborrheic dermatitis may be present. There is no atrophy.

From acute disseminate *lupus erythematosus* one must sometimes distinguish *erysipelas*. This is asymmetrical unless it begins in the median line, and it spreads rapidly with a sharply elevated, glossy, hard surface upon which vesicles or bullae may appear. There is usually only one patch, fever is high, and leukocytosis is marked.

Severe febrile *erythema multiforme* seldom involves the face and the mouth involvement is severe in comparison to facial participation. Leukocytosis and positive blood cultures may decide. The lesions of *erythema multiforme* on the extremities often enlarge rapidly in concentric circles.

TREATMENT

The treatment of erythematous *lupus* has three objectives:

1. To prevent scars in discoid cases.
2. To prevent exacerbations of either chronic form.
3. To save life in the acute phase.

Treatment of Chronic Discoid and Disseminate Lupus

The first objective is attained by prompt clearing of the discoid eruption. The patient should understand at the outset that scars are apt to occur, if not already present. Just as the laity frequently mistakes stains for scars, so they in rare instances fail to recognize the scars already in evidence.

Rest is an important factor in treatment of any case of erythematous lupus. Many patients afflicted with the chronic form are of the nervous atonic type and constantly overtax themselves. Becker, in a discussion of the paper of Ludy and Corson,⁶ has wisely emphasized this point.

For the incipient chronic case, first try soothing the lesions with *cool wet dressings* of cuticolor lotion,* saturated solution of boric acid or one part of liquor alumini subacetatis in 16 parts of water. Rarely an oncoming patch will subside under such management and it is always wise to treat young eruptions with gentle methods until their character has been established.

If the lesion proves resistant or if evidently chronic when first seen, mild stimulation, such as is afforded by *lotio alba* or the new *lotio sulfurata* of Abramowitz,¹⁵ may be tried.

Lotio sulfurata

Solution of sulfurated lime, NF., filtered	30.0
Saturated solution of zinc sulfate, filtered	...	20.0
Glycerin	5.0
Mix and let stand. Shake and dab on the spots once a day. Let it dry on.		

If not enough effect is obtained from one or the other of these lotions dabbed on once a day, brisk scrubbing with soap and water before applying the lotion may enhance the effect.

A more indolent patch may be stimulated by Small's combination of 1 part *phenol* and 4 parts *lactic acid* painted on after cleansing the skin with ether. This can be repeated once a week if the irritation of the previous treatment has subsided.

Still more vigorous is the action of a stick of *carbon dioxide snow* pressed on for from five to twenty seconds, depending on the indolence of the lesion. In the case of very old skins and those which have been previously treated with radium or roentgen rays, special care must be taken, for they sometimes react excessively. A preliminary freezing for one second may be tried.

In the treatment of a systemic disease, as erythematous lupus undoubtedly is, it seems reasonable to favor measures

* Cuticolor powder of Fantus and Dyniewicz in bentonite suspension, an improvement on calamine lotion.¹⁴

influencing the whole organism rather than the skin alone. The importance of rest has already been emphasized. Diet may be the means of exerting a decidedly beneficial action. Since the introduction by Gerson of the *salt-poor, raw fruit and vegetable diet* for tuberculosis of the skin it has proved of great benefit in certain cases of lupus erythematosus. Most of them have been of the chronic type, but Löhe¹⁶ mentions a case of acute erythematous lupus which, after nine weeks of a salt-free diet with a preponderance of raw foods, was entirely healed and the patient had gained 4.5 kg. in weight. Urbach¹⁷ also reports good results in some cases, none in others. He outlines the diet and discusses its *modus operandi*.

Anderson and Ayres¹⁸ mention several cases of the disease benefited by a raw fruit and vegetable diet.

The Whitehouse method of giving *iodoform*, 0.06 gm. (1 grain) three times a day by mouth, is praised by some. *Quinine* by mouth, pushed to the limit of tolerance, is also credited with good results. Holländer¹⁹ introduced the internal administration of quinine combined with local application of iodine. He gives a precautional first dose of 0.05 gm. (about 1 grain) to uncover a possible sensitiveness to the drug, and if none is present he administers 0.5 gm. (8 grains) of quinine chloride or sulfate three times a day after meals. Five or ten minutes after taking this the patient paints each discoid lesion with tincture of iodine, applying several coats. Two such paintings each day are sufficient and after five or six days of treatment a rest is necessary. A crust forms and if, after this falls, a smooth skin is not left, the treatment must be repeated. This method sometimes produces excellent results.

Salicin, 0.6 gm. (10 grains) to 1 gm. (15 grains) three times a day by mouth, or *bitumen sulfonate* (ichthyol) in doses of 0.12 gm. (2 grains) three times a day have been praised. Many other drugs have been used with occasional good results. Among those mentioned in the textbooks is *potassium iodide* which I mention only to warn of danger in administering it to patients with disseminate lupus erythematosus with kidney damage. I have seen disaster follow

promptly after three doses of 0.3 gm. (5 grains) in such a case.

The intramuscular injection of the patient's own blood or blood serum is a mild form of *foreign protein therapy* that sometimes produces decided benefit; 5 to 20 cc. may be given every five to seven days for six to eight doses or longer. A mild febrile reaction sometimes occurs after the first dose, but it has never been troublesome in my experience.

Another mild form of treatment is that suggested by Goeckerman:²⁰ filtered *roentgen rays* to the lymphatic glands. He reports excellent results in a large percentage of cases and, in some, astonishingly prompt results. This is substantiated by O'Leary²¹ and I have seen excellent results in a few cases from this treatment.

Reute²² in 1913 showed that lupus erythematosus is highly responsive to treatment with *gold salts*. This method, because it is more consistently successful than any other, has become the favorite form of treatment—so popular that some seem to regard it as the only one. This is far from the truth. It is a very dangerous drug in acute cases of erythematous lupus and in the subacute disseminate cases it must be employed, if at all, with the greatest care.

There are many preparations of gold in use, but in this country gold and sodium thiosulfate introduced by Schamberg and Wright²³ is by far the most popular. Since early days the customary dosage has been reduced so that now 50 mg. once a week intravenously is the maximum. According to the nature of the case, from 1 to 50 mg. are given intravenously once a week for twenty weeks or longer if needed. Frequent examination of the urine, blood and skin must be made and functional tests of the excretory ability of the kidney and the functioning of the liver will not be amiss. According to Throne and Myers,²⁴ repeated findings of high blood sugar and low blood chloride levels warn of retention of heavy metal. In cases in which retention is present, treatment with sodium thiosulfate gives excellent results.

Untoward reactions to gold are much like those made too familiar to us by the arsphenamines. Fever, nausea and vomiting, diarrhea and stomatitis may occur soon after the in-

jection or days or even weeks thereafter, lasting a few days or many weeks. Pruritus, erythema, urticarial, papular or vesicular eruptions may eventuate in exfoliative dermatitis. Erosions and ulcers may occur upon the mucous surfaces. Aplastic anemia, purpura with hemorrhages into the skin and from the internal organs, leukopenia and even agranulocytosis may occur.

In spite of all this the proportion of toxic accidents is low compared to the great number of injections given.

Bismuth given as for syphilis is also helpful in the chronic cases. It is less toxic and less active than gold. It may be given in courses alternating with those of gold salts.

Treatment of Acute Exacerbations and Acute Erythematous Lupus

Acute exacerbations and acute erythematous lupus constitute a much more difficult problem. *Rest* may be aided by a darkened room, cool compresses to the face as recommended for the chronic cases, and tepid baths in starch or oatmeal water. The *diet* should be as nutritious as the state of the gastro-intestinal tract permits, with, of course, no alcohol or condiments included.

All remarks in the presence of the patient must be encouraging. Some responsible member of the family should be warned of the danger. All possible means of investigation that do not unduly tire the patient should be instituted, but if infectious foci are found, they should not be disturbed. Attempts at eradication of such foci during the acute phase of the disease are dangerous.

Small *blood transfusions*, repeated frequently, are perhaps the most effective means of combating acute lupus erythematous.

Sulfanilamide has been successful in a number of instances. Wile and Holman²⁵ treated seven cases with it, with decided and lasting benefit in one discoid case in exacerbation and temporary benefit in two others. Their review of the literature shows that improvement, sometimes remarkable, occurred in nine of twenty-one cases. As was to be expected, it was greatest in the exacerbations of discoid cases, but benefit was seen in several acute disseminate cases. Even though the good

effect was only temporary, these reports are encouraging. The case of Wallenberg, later treated by Wile and Holman, was twice brought to remission by sulfanilamide.

Gold, if used at all in such cases, must be given in minute doses with great care. Wile and Holman²⁵ report a case which after failure of sulfanilamide yielded to gold therapy. On the other hand, their most successful case was one of discoid lupus that became disseminated during a course of gold therapy and yielded to sulfanilamide.

Rose and Pillsbury⁷ used pentose nucleotide, lyophilized convalescent scarlet fever serum, polyvalent antistreptococcus serum, vitamin B concentrate and plasmochin in addition to the methods already discussed, with no encouraging results.

The treatment of acute disseminate lupus erythematosus has been at best a heart-breaking job. However, the greater facility for obtaining blood transfusions today and the occasional success of sulfanilamide have slightly improved the chance of relieving the pitiable victims of this disease.

BIBLIOGRAPHY

1. Kren, O.: Über Lupus Erythematodes der Lippenroths und der Mundschleimhaut. Arch. f. Derm. u. Syph., 83: 13, 1907.
2. Stickney, J. M.: Systemic Involvement in Lupus Erythematosus. Proc. Staff Meet. Mayo Clin., 15: 680, 1940.
3. Slocumb, C. H.: Arthralgia and Arthritis of Lupus Erythematosus. *Ibid.*, 15: 683, 1940.
4. Maumenee, A. E.: Retinal Lesions in Lupus Erythematosus. Am. J. Ophth., 23: 971, 1940.
5. Keil, H.: Dermatomyositis and Systemic Lupus Erythematosus. Arch. Int. Med., 66: 109, 1940.
6. Ludy, J. B. and Corson, E. F.: Lupus Erythematosus. Arch. Derm. & Syph., 37: 403, 1938.
7. Rose, E. and Pillsbury, D. M.: Acute Disseminate Lupus Erythematosus, A Systemic Disease. Ann. Int. Med., 12: 951, 1939.
8. Baehr, G., Klemperer, P. and Schiffrin, A.: A Diffuse Disease of the Peripheral Circulation. Tr. Assoc. Am. Phys., 50: 139, 1935.
9. Pusey, W. A. and Rattner, H.: Use of Adrenal Substance in Cases of Dermatitis Which May Have a Menstrual Factor. Arch. Derm. & Syph., 31: 865, 1935.
10. Goeckerman, W. H.: Is Lupus Erythematosus Discoïdes Chronicus due to Tuberculosis? *Ibid.*, 3: 788, 1921.
11. Goeckerman, W. H., Osterberg, A. E. and Sheard, C.: Eczema Solare in a Case of Hematoporphyria. *Ibid.*, 20: 501, 1929.
12. Belote, G. H.: Lupus Erythematosus Disseminatus, Its Present Status. *Ibid.*, 39: 793, 1939.

13. Reifstein, E. C., Reifstein, E. C., Jr. and Reifstein, G. H.: A Variable Symptom Complex of Undetermined Etiology with Fatal Termination. *Arch. Int. Med.*, 63: 553, 1939.
14. Fantus, B. and Dyniewicz, H. A.: Cuticolor Preparations. *J. Am. Phar. Assoc.*, 27: 878, 1938.
15. Abramowitz, E. W.: A New Lotio Sulfurata. *Arch. Derm. & Syph.*, 28: 709, 1933.
16. Löhe: Erfolg der Kochsalzfreien Diät bei Hauttuberkulosen. *Zentralbl. f. Haut u. Geschl. Kr.*, 32: 544, 1930.
17. Urbach, E.: Skin Disease and Nutrition, English Trans. by F. R. Schmidt, 1932. Maudrich, Vienna, p. 182.
18. Anderson, N. P. and Ayres, S.: Light Sensitive Dermatoses. *J.A.M.A.*, 103: 1279, 1934.
19. Holländer, E.: Der Lupus Erythematoses. *Berl. Klin. Woch.*, 39 (30): 705 (July 28) 1902.
20. Goeckerman, W. H.: The Treatment of Lupus Erythematosus by Filtered X-Ray to the Gland-bearing Regions of the Body. *Med. J. & Record*, 120: 530, 1924.
21. O'Leary, P.: Prognosis and Treatment of Lupus Erythematosus. *Proc. Staff Meet. Mayo Clin.*, 15: 686, 1940.
22. Reute, A. E.: Über den Wert des Aurium Kalium Cyanatum bei der Behandlung des Lupus Erythematoses. *Deutsch. Med. Woch.*, 39: 1727, 1913.
23. Schamberg, J. F. and Wright, C. S.: The Use of Gold and Sodium Thiosulphate in the Treatment of Lupus Erythematosus. *Arch. Derm. & Syph.*, 15: 119, 1927.
24. Throne, B. and Myers, C. N.: Psoriasis. *New York State J. Med.*, 26: 914, 1928.
25. Wile, U. and Holman, H. H.: Acute Disseminate Lupus Erythematosus, Its Treatment with Sulfanilamide and Allied Products. *Arch. Derm. & Syph.*, 42: 1059, 1940.

VITAMINS IN DERMATOLOGY

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VITAMINS are organic substances which, in very minute quantities, are essential to good health and normal growth. The body is unable to synthesize them so they must be present in the food. Vitamin D is an apparent exception in that it is produced under optimal conditions by the action of sunlight on the human skin. When it is not so produced it must be added to the diet.

The subject of vitamins and their role in health and disease is fascinating not only to the biological and medical scientist but to the lay public as well. Americans have an intense interest in public health problems. The mysterious role of substances, present in extremely minute quantities in our daily food, in influencing our well-being has a unique appeal. Over the airways, in the public press, through the current magazines flows a constant stream of information and speculation about these new marvels. As a natural corollary, misinformation, groundless speculation and broad claims with no basis in fact have followed in the wake of scientific investigation. Commercial exploitation of this popular interest has not been lacking. Self-medication with vitamin preparations on an enormous scale has resulted. Fortunately very little harm has occurred. Rational attempts are also being made to restore to everyday foods essential vitamins removed by processing, such as thiamine chloride in white flour. The war has stimulated these efforts at home and abroad.

PRESENT STATUS OF THE VITAMIN PROBLEM

In order that we might properly advise our patients and use this new knowledge effectively in our practice a brief summary of the present status of the vitamin problem seemed

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in order. The accretion of new knowledge occurs so rapidly and the pertinent literature is so vast that any presentation of the subject is bound to be obsolescent by the time it appears in print. This situation is largely a culmination of patient, painstaking work carried on by the biochemists over a long period. The vitamins are rapidly being isolated and artificially synthesized in quantities sufficient for large scale experimentation and clinical study.

On closer examination, however, we find that accurate, detailed knowledge of the *physiological action* of the individual vitamins has not always kept pace with our knowledge of either the chemical structure or the clinical manifestations. Doubtless great advances will be made in this field which will lead to more effective therapeutic applications.

Accurate *quantitative measurement* of the vitamins has presented many difficulties. Bio-assay, although absolutely essential, has been tedious, beset with pitfalls and has had a considerable margin of error. With the chemical isolation and synthesis of the vitamins we are on our way to having a measuring rod which the clinician can use more effectively. Methods for assaying the vitamin content of the body at any given time are much needed. Some vitamins like thiamine are stored in very small quantity and must be furnished daily. Others like vitamin C are stored in sufficient amounts to last for months. Development of new methods for vitamin assay in the human will undoubtedly be one of the next important developments.

Splitting up the vitamin B complex into so many components and the study of their individual action must not blind us to the fact that in nature vitamin deficiencies are rarely single but multiple and that in therapy *natural products* may have an advantage which is difficult to explain. There is undoubtedly a considerable synergistic action of one vitamin on another. On the other hand, with the multiplicity of commercial products it is essential that we have some knowledge of the optimal requirements of the various vitamins included in a polyvalent vitamin product.

Undoubtedly the ideal situation for the healthy individual would be to supply the vitamin requirements in natural foods.

Consequently a knowledge of the vitamin content of common foods, the effect of processing, storage and cooking on this content are of prime importance.

PRIMARY AND SECONDARY VITAMIN DEFICIENCIES

Rhodes¹ in an address before the Institute of Medicine of Chicago, distinguished between primary and secondary vitamin deficiencies. The following outline is loosely based on his classification.

Primary deficiency is due to an inadequate supply of vitamins in the diet. This may be due to poverty, war conditions, social habits, dietary fads and occasional special diets for gastro-intestinal disorders, such as functional bowel disturbance and gallbladder disease.

Secondary deficiencies may be produced in several ways:

1. Loss of vitamins from the intestinal canal by increased mobility or in chronic diarrhea.

2. Incomplete absorption through the intestinal tract as the failure to absorb vitamin K in the absence of bile salts and the necessity for normal fat absorption for vitamin A or the inability to absorb vitamin D in steatorrhea.

3. The lack of a bodily factor required to convert vitamins to a usable form. In pernicious anemia an enzyme is lacking in the gastric juice which when present converts something in yeast to a hematopoietic factor. Also the inability of damaged liver cells to convert carotene to vitamin A or utilize K in production of prothrombin.

4. Increased demands for vitamins due to (a) fever, (b) increased metabolism as in exercise, (c) hyperthyroidism, (d) pregnancy and (e) lactation.

5. Inhibition of vitamins by infections and by other toxins.

6. Endocrine dysfunction. Sutton and Ashworth were able to produce pellagra at will in certain patients by withholding or administering an anterior pituitary extract or adrenal extract. Thyroid may be useful in splitting carotene.

7. Personal high requirements are undoubtedly of importance in some individuals. The physiological explanation still escapes us.

BIOLOGIC OXIDATION

The process of biologic oxidation is an important one in understanding the physiological action of the vitamins. At least three of the B complex, *i.e.* thiamine, riboflavin and nicotinic acid, and possibly two others, pyridoxine and pantothenic acid, are concerned with biologic oxidation. Vitamin C is a biologic oxidant in plants. Its physiologic role in humans is obscure though its deficiency manifestations are well known. It is very possible it has a place in the oxidation process. Likewise vitamin A may possibly play some part in the oxidation of unsaturated fatty acids. I would recommend to everyone the lucid and fascinating account of biologic oxidation in Szent-Györgyi's little book.

The source of all energy in the cell is the oxidation of foodstuffs. If the total energy of carbohydrate, for instance, was released in one step the heat produced would burn the cell. Consequently it must be released step by step. Chemically speaking, the withdrawal of hydrogen from an organic molecule is oxidation. An elaborate system of hydrogen acceptors and donators is used to pass the hydrogen from higher to lower energy levels—a hydrogen "bucket brigade" as it has been called. A small amount of energy is released at each step. Some of the vitamins, though present in extremely minute quantities, are phosphorylated, and unite with bearer proteins to form enzymes which activate important steps in this process of biologic oxidation. When deficient or absent the orderly process of oxidation is interrupted and profound disease symptoms are initiated, such as pellagra and beriberi.

VITAMIN A

Absorption and Metabolism of Vitamin A and Carotene.—Vitamin A is an unsaturated alcohol. It may be found in foods, as the vitamin itself, or one of its precursors, the carotenoid pigments. The absorption and metabolism of the provitamins and vitamin A are of extreme practical importance. Vitamin A, an alcohol, in the presence of fatty acids, is converted into a fatty acid ester. A normal amount of bile must be present to insure its absorption. Carotene is transported across the intestinal wall only when there is absorp-

tion of normal amount of fat, in the presence of bile. Hence, any disease which causes diminished flow of bile or interferes with fat digestion will interfere with the absorption of vitamin A and its provitamins.

Much still remains to be learned about the absorption of vitamin A and carotene. There is experimental evidence that the thyroid may play an important part. Other factors remain to be discovered which inhibit the proper absorption. In some individuals there appears to be an inability to transform carotene into vitamin A. Popper² has demonstrated with the fluorescent microscope that vitamin A is stored in the Kupffer cells and parenchymal cells of the liver, in the body fat, in the adrenals and the gonads. The liver is the most important storage organ and the ability to store vitamin A may be inhibited by disease. Not infrequently there is evidence in the skin of vitamin A deficiency in cirrhosis of the liver.

Unit. The unit of vitamin A is the amount necessary to produce the physiological effect of 0.0006 mg. of pure beta-carotene.

Sources. Green growing leaves are the best food sources. The yellow vegetables contain considerable amounts. Oleum percomorphum contains 60,000 U.S.P. units per gram, approximately 1 cc. If the dropper used requires 3 drops for 1 minim. there would be 1333 units per drop. Plain haliver oil furnishes 55,000 units per gram, or 1200 per drop. Cod liver oil contains 600 units per gram, or 2400 per teaspoonful. Capsules of high concentration, i.e., 25,000 units and 50,000 units of vitamin A, are available and relatively inexpensive.

The requirements for a normal adult are 5000 units daily. During pregnancy and lactation this is increased to 8000 units.

Vitamin A Deficiency

The exact physiological action of vitamin A is obscure. It is essential to the production of visual purple. Its deficiency results in *night blindness*. Tests for dark-adaptation are being perfected to determine vitamin A deficiency. Other deficiency manifestations are found in many epithelial structures, resulting in *keratinization* similar to that found in the epi-

dermis, and to *hyperkeratosis* of the epidermis itself. The skin becomes dry and rough and papules appear due to the keratinization of the follicular openings. Atrophy of the sweat glands and keratinization of their ducts account for lack of sweat. Comedones form and the sebaceous glands show both keratinization and metaplasia. Frazier and Hu³ reported such skin conditions in undernourished Chinese, to which they gave the name *toad skin* or *phrynoderma*. Lowenthal⁴ described similar skin changes associated with night blindness and xerophthalmia in South African prisoners on a diet low in vitamin A. They were cleared up by the administration of cod liver oil. While night blindness responds quickly to the administration of vitamin A, the skin changes are slow to yield and require continuous treatment over a period of months.

Therapeutic Uses

Follicular Hyperkeratoses.—Many clinical entities characterized by follicular hyperkeratosis, with dryness of the skin due to diminished oil and sweat, have been described by clinicians. *Keratosis pilaris*, one of these conditions characterized by follicular plugging most marked on the external surfaces of the arms and on the legs, usually clears up in the summer and is improved by the administration of thyroid. *Lichen spinulosus*, another disorder not influenced by season, possibly of toxic origin, characterized by horny follicular spines, usually grouped and scattered irregularly over the body, is a rarer condition. Lehman and Rappaport⁵ suggested that such conditions might respond to large doses of vitamin A. Doses of 150,000 units daily should be used. It is our experience that disorders characterized by hyperkeratosis, such as keratoderma of the palms and soles, are benefited by the administration of vitamin A.

Pityriasis Rubra Pilaris.—This is a relatively rare chronic skin disorder characterized by the appearance of conical keratotic follicular papules and hyperkeratotic plaques on the palms, soles, knees and elbows, and associated with a fine white scale of the scalp and at times of the face. In more advanced cases these papules may coalesce to form a general-

ized exfoliating erythroderma. The disorder usually begins in the first three decades of life; incomplete remissions are the rule. Occasionally one sees a patient with similar skin changes which appeared for the first time in middle or late life. Brunsting⁵ studied three cases of this type appearing in middle age. In each case there was diminished dark-adaptation and in one a carotinemia, indicating an inability to split carotene and form vitamin A. All these patients responded to the administration of vitamin A, with disappearance of night blindness and a gradual improvement in the skin condition. We have had a similar experience and would recommend thyroid administration, if there are no contraindications, as a valuable adjunct.

The milder atypical cases, characterized by palmar and plantar keratoses with yellowish-red plaques on the elbows and knees, have responded particularly well. The dose of vitamin A should be large, at least 150,000 units daily. The topical administration of cod liver oil is of value in hastening the absorption of the plaques.

Gross⁷ finds the intramuscular injection of crude liver extract three times a week also of great value in cases of this type.

Darier's Disease.—As its other name, keratosis follicularis, indicates, this rare disorder is characterized by dyskeratosis which manifests itself clinically by follicular keratotic papules which become covered by a greasy grayish or brownish crust. It usually begins in childhood and is slowly progressive. Peck, Chargin and Sobotka⁸ have demonstrated in four cases that the vitamin A content of the blood serum is low, but the carotene content normal. In two cases there was diminished light adaptation. The administration of 200,000 units of vitamin A daily caused a gradual disappearance of the eruption in three of the four cases. They postulate an hereditary inability in these patients to absorb vitamin A or to transform carotene into vitamin A. We have had no personal opportunity to test this treatment, but feel certain it is a valuable contribution to the therapy of an otherwise very resistant skin disorder.

A combination of vitamins A and D in the form of cod

dermis, and to *hyperkeratosis* of the epidermis itself. The skin becomes dry and rough and papules appear due to the keratinization of the follicular openings. Atrophy of the sweat glands and keratinization of their ducts account for lack of sweat. Comedones form and the sebaceous glands show both keratinization and metaplasia. Frazier and Hu³ reported such skin conditions in undernourished Chinese, to which they gave the name *toad skin* or *phrynoderma*. Lowenthal⁴ described similar skin changes associated with night blindness and xerophthalmia in South African prisoners on a diet low in vitamin A. They were cleared up by the administration of cod liver oil. While night blindness responds quickly to the administration of vitamin A, the skin changes are slow to yield and require continuous treatment over a period of months.

Therapeutic Uses

Follicular Hyperkeratoses.—Many clinical entities characterized by follicular hyperkeratosis, with dryness of the skin due to diminished oil and sweat, have been described by clinicians. *Keratosis pilaris*, one of these conditions characterized by follicular plugging most marked on the external surfaces of the arms and on the legs, usually clears up in the summer and is improved by the administration of thyroid. *Lichen spinulosus*, another disorder not influenced by season, possibly of toxic origin, characterized by horny follicular spines, usually grouped and scattered irregularly over the body, is a rarer condition. Lehman and Rappaport⁵ suggested that such conditions might respond to large doses of vitamin A. Doses of 150,000 units daily should be used. It is our experience that disorders characterized by hyperkeratosis, such as keratoderma of the palms and soles, are benefited by the administration of vitamin A.

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feet, associated usually with a general eruption of small red papules. These little patients rub and bite their hands, have an intense photophobia and are extremely miserable.

Madden¹⁰ found thiamine of value in the treatment of *psoriasis*. We have used it but find it difficult to interpret the results because it was used in conjunction with other local measures.

Riboflavin

This is a water-soluble sugar dye which when phosphorylated unites with a bearer protein to form the yellow oxidation enzyme of Warburg. By changing the bearer protein it may become the constituent of several enzymes. These enzymes act to transfer hydrogen in various steps of biologic oxidation. The adult *requirement* of riboflavin is 2.2 to 3.3 mg. daily, depending on activity. The best food *sources* are liver, kidney, lean beef, pork, eggs, milk, cheese, flour and greens.

Occasionally we have seen in the wards at Cook County Hospital a case of riboflavin deficiency with classical symptoms of magenta-colored tongue, redness and exfoliation of the lips, maceration of the labial angles, *perlèche* associated with seborrheic scaling of the nasolabial folds and the temples, and a follicular keratosis of the forehead, malar regions and chin. These cases have occurred in patients on inadequate intake due to abdominal malignancy and respond well to the administration of riboflavin. Unfortunately, not all cases of *cheilitis*, *perlèche* and *seborrheic dermatitis* of the nasolabial angles and ears respond to riboflavin administration, even when given in large doses; in fact, very few of them do. It may be possible that the administration of the whole B complex parenterally as suggested by Gross would be of greater value. Riboflavin has proved efficient in the management of *rosacea keratitis* but not of particular value in the skin manifestations of *acne rosacea*.

The *therapeutic dose* is 15 to 25 mg. daily by mouth.

Nicotinic Acid

Nicotinic acid is water-soluble and heat-stable. It is an essential component of an enzyme which acts as a hydrogen

liver oil ointment has been found to be antiseptic and an excellent stimulant to epidermis formation. It is widely used in the treatment of burns and we have found it useful in the treatment of sluggish ulcers.

VITAMIN B COMPLEX

Much of the confusion inherent in the serial denomination of the components of the B complex has been dissipated by their chemical identification. Three of these components, thiamine, riboflavin and nicotinic acid, are concerned with biologic oxidation and two more, pantothenic acid and pyridoxine, are probably similarly concerned.

Thiamine

This heat-labile, water-soluble fraction of vitamin B complex is essential to the oxidation of carbohydrates. When insufficient or absent, polyneuritis, cardiac symptoms or mental symptoms may occur. Thiamine is poorly stored, so the daily intake must be adequate. The daily *requirement* is 1.5 to 2.3 mg., depending on activity. Modern diets are apt to be low in thiamine content because it is removed in the processing of wheat and other cereals. Due to the stimulus of the war, the United States Government is perfecting arrangements to restore thiamine to white flour. Patients who are on intravenous glucose require large amounts of thiamine. It should be supplied, if necessary, parenterally.

In spite of its remarkable success in the treatment of the *polyneuritis* of diabetes, pregnancy, alcoholism and beriberi, thiamine has proved of no value in *arsenical peripheral neuritis* and of little value in the lightning pains of *tabes*. We have not found it of great value in controlling *post-zoster neuritis*, although we consider it a useful adjunct. Its most successful use is reported in the treatment of *acrodynia*. Durand, Spickard and Burgess⁹ recommend the intramuscular injection of 6 mg. of thiamine daily for six days and then every other day until the disorder is under control. We have had no personal experience but other authors have reported its great value in the treatment of this rare disorder of infants which is characterized by cyanosis, erythema and edema of the hands and

variety we have seen no results from its use. In one case of subacute disseminated lupus erythematosus 50 mg. of nicotinic acid amide administered parenterally three times a week caused a remarkable remission. In a number of other cases it has seemed of no value.

Pyridoxine

Pyridoxine (vitamin B₆) is one of the most recent components of the B complex to be isolated. Vilter, Ering and Spies¹⁴ reported the partial remission of severe *arsenical polyneuritis* with use of pyridoxine. They administered 20 mg. in physiological saline intravenously twice a day for three days. The improvement was more spectacular when 50 mg. of alpha tocopherol (vitamin E) was given intramuscularly in conjunction with B₆. We have had no occasion to try this method but think that it certainly warrants trial in cases of arsenical polyneuritis.

Other Vitamin B Components

Other components of the B complex, pantothenic acid, biotin, the anti-gray hair factor which prevents the graying of hair in rats, etc., have not been studied long enough to suggest definite dermatologic use. There can be no question, however, of their importance in the B complex.

Liver Extract Parenterally

Paul Gross¹⁵ has recently reviewed his extensive experience with the use of vitamin B complex administered parenterally twice a week, in the form of a liver extract, which was especially assayed for the presence of all fractions of the B complex. He reports four cases of extensive eruption in the folds of the skin of the type sometimes called *seborrheic eczema* and sometimes called *infectious dermatitis*, which were resistant to all other therapy but responded to the intramuscular injection of crude liver extract. He also reported two cases of extensive *monilia infection* of the natural folds of the skin which also responded to the same treatment. Free gastric hydrochloric acid was absent or greatly diminished in all these cases.

donator and acceptor in the process of biologic oxidation. The daily *requirement* of nicotinic acid is 25 mg. The best food *sources* are fresh beef, pork, liver, kidneys; there is a small amount in milk and eggs; yeast in a very valuable source.

The dramatic story of the elucidation of the main factor in the etiology of *pellagra* is well known. Goldberger's proof of its dietary origin has even been the subject of a recent radio drama. Elvehjem's observation that nicotinic acid relieved black tongue in dogs, the equivalent of human *pellagra*, led Spies and his co-workers to the demonstration of the curative power of this important biologic oxidant in clinical *pellagra*, thus setting the capstone to years of investigation of this important disease. *Pellagra* is a multiple vitamin deficiency in nearly every case. The majority of cases that we see occur in chronic alcoholics, with coincidental restricted diet. Endocrine disturbances may cause an abnormally high individual requirement, as shown by Sutton and Ashworth.¹¹ Nicotinic acid deficiency may be due to abnormal loss of contents from the intestinal tract due to diarrhea, amebic dysentery, typhoid fever, or ulcerative colitis. Infections and chronic systemic disease may inhibit vitamin function.

In severe cases of *pellagra* with acute symptoms we have given 500 mg. of nicotinic acid dissolved in 5 per cent dextrose-physiologic saline solution as a continuous drip; in less severe cases 500 mg. in ten divided doses by mouth. This is combined with a high vitamin and high caloric diet as soon as possible. Nicotinic acid amide causes less flushing and discomfort immediately after administration and is preferable to nicotinic acid per se.

Lynch¹² has suggested the administration of 100 mg. of nicotinic acid daily as valuable treatment in *acne vulgaris*. Several authors have recommended nicotinic acid in treatment of *toxic symptoms* due to sulfonamide drugs. We use it in doses of 100 mg. of nicotinic amide by mouth daily for all acute drug reactions.

Kühman¹³ advocated the administration of nicotinic acid for treatment of *lupus erythematosus*; in the chronic discoid

as well as subperiosteal and intramuscular hemorrhages and bleeding gums.

The *Rumpel-Leeds test for capillary fragility* is an excellent clinical test. A circle 2.5 cm. in diameter is drawn with its upper edge 4 cm. below the cubital fold on the flexor aspect of the forearm. With a blood pressure cuff, a pressure midway between diastolic and systolic is sustained for fifteen minutes; after five minutes, the petechial hemorrhages are counted. Ten or less are normal; 10 to 20 borderline; 100 or more are strongly positive. A positive test may occur in scarlet fever, thrombocytopenic purpura, anemia and other diseases that are easily ruled out clinically. Fully developed cases of scurvy are frequently seen in large hospitals like the Cook County Hospital. However, it is the subclinical states of hypovitaminosis that are particularly interesting to the clinician.

Therapeutic Uses

Hyperkeratotic Lesions.—It has long been thought that dry follicular, keratotic papules might be a manifestation of vitamin C deficiency. Crandon, Lund and Dill¹⁶ report a remarkable voluntary abstention from vitamin C in one of their number who was on an otherwise normal diet. After 132 days the appearance of keratotic papules over the buttocks was the first objective finding; thirty days later petechial hemorrhages appeared and at 183 days there was definite absence of wound healing. One may conclude from this experiment that in the treatment of hyperkeratotic lesions discussed under vitamin A, an adequate supply of ascorbic acid should be included in the diet.

Drug Sensitivity.—The influence of a low ascorbic acid diet on the production of sensitivity is still a moot point. Sulzberger and Oser¹⁷ demonstrated that large doses of vitamin C diminished the susceptibility of the guinea pig's skin to sensitization with neoarsphenamine. Chapman and Morrell¹⁸ reported exactly the opposite findings. Recently MacDonald and Johnson¹⁹ could find no relation between blood ascorbic acid levels and sensitivity to repeated intradermal injections of neoarsphenamine in the guinea pig. It is possible that other factors, still undiscovered, may explain these varying results. Despite the contradictory experimental reports, we believe it

Any new method of value in the treatment of these extremely resistant conditions is welcome. However, we have not had enough experience to evaluate these suggestions.

The parenteral administration of crude liver extract is recommended as a valuable adjunct in the treatment of arsenical reactions.

VITAMIN C

Vitamin C, or *ascorbic acid*, is water-soluble and extremely sensitive to oxidation. Only man, the primates and the guinea pig do not synthesize vitamin C. In plants it acts as a hydrogen transport agent in biologic oxidation, but in animals its chemical action is not understood.

Requirements.—Young children require 40 to 100 mg. daily and adults 5 mg. One milligram is the equivalent of 20 international units. Pregnancy, lactation, acute infections and heavy work increase the requirements. It is well stored and persists for many weeks.

Sources.—Citrus fruits are the richest source; 50 mg. are found in 100 cc. of orange juice or 250 cc. of canned tomato juice. Fresh greens contain considerable amounts, but crushing or storage in warm places soon oxidizes the supply. Cooking should be started in hot water and copper utensils never used.

Vitamin C Deficiency

Crandon, Lund and Dill¹⁶ have demonstrated that a blood plasma level of zero does not produce scurvy or approach it, but a level of zero in the white cell platelet layer of centrifuged plasma coincides with the first appearance of skin lesions.

The primary effect of vitamin C deficiency occurs in the intracellular substances of certain mesenchymal derivatives. The ground substance does not differentiate; for instance, in wound healing in the absence of ascorbic acid, fibroblasts are present but do not differentiate into collagen fibers; hence, its use is advocated by surgeons to promote wound healing. In the absence of ascorbic acid the bones and teeth cease to develop properly. The marked increase in capillary permeability results in the clinical manifestation of *hemorrhage* as perifollicular petechiae, subcutaneous ecchymoses

The principal action of vitamin D is to increase the intestinal absorption of *calcium*. Its action is related to the calcium and phosphorus content of the diet and to its acid-base value, as well as to the activity of the parathyroids and the thyroid. There is experimental evidence to show that it has a specific action on cell activity with an increase of cellular metabolism. It stabilizes the calcium and phosphorus metabolism. The exact chemical methods by which this is accomplished in the cell are still not understood.

Units.—The international unit is the vitamin D activity of 0.025 mg. of crystalline vitamin D.

Human Requirements.—The requirement of adults is undetermined. During lactation and pregnancy 800 units are required daily with an adequate calcium and phosphorus intake; during adolescence and infancy 400 units to 800 units are required daily.

Sources.—(a) Exposure of the skin surface to ultraviolet light or to solar radiation of the proper wave length. (b) Foods: fish with large amounts of body oil; small amounts in eggs and cream.

The average diet contains insufficient vitamin D. If solar exposure is inadequate, it must be supplemented in the form of (c) cod liver oil, U.S.P., which contains 340 units per teaspoonful; (d) viosterol in oil 40,000 units per teaspoonful, approximately 220 units per drop. Viosterol can also be dispensed in propylene glycol in the form known as Drisdol and it has no fishy taste. It can also be fortified with vitamin A in the form of (e) haliver oil and viosterol. (f) Milk can be fortified (1) with viosterol 400 units per quart, (2) irradiated, 135 units per quart, and (3) yeast milk from cows fed with yeast.

The absorption of vitamin D may be inhibited by the lack of bile and by the formation of calcium soaps in fat disturbances.

Therapeutic Uses

Various incentives contributed to the extensive trial of vitamin D in the treatment of dermatologic conditions. Disorders like *psoriasis* and *acne vulgaris* usually improve under

is sound policy to administer adequate quantities—at least 100 mg. daily—of ascorbic acid during intravenous therapy with gold, arsphenamine and during the oral administration of the sulfonamide group of drugs.

Pigmentary Disorders.—Cornbleet²⁰ emphasizes the deposit of pigment in the skin when the body stores of ascorbic acid are exhausted. Morowitz²¹ claimed that the administration of vitamin C in Addison's disease removes the pigment. We have had no opportunity to test these findings in pigmentary disorders.

VITAMIN P

Szent-Györgyi and associates²² claimed to have found in natural vegetable juices and citrus fruits a vitamin P made up of two flavones, hesperidin and eriodictyol glucoside. He believes the special function of vitamin P is to regulate vascular permeability. Kugelmass²³ has found vitamin P concentrate of value when administered orally to two children with *allergic purpura* and in another infant with *nutritional purpura*. Further studies on this question are much needed. Goldfarb²⁴ has reported favorable results in thirty-one patients with *psoriasis* treated with *citrin*, the vitamin P concentrate of lemon. Scarborough²⁵ would distinguish between the ecchymoses and bleeding gums due to vitamin C deficiency and the petechial circumpilar hemorrhages due to deficiency of vitamin P. The clinical experience of any one man is still too limited to permit broad generalization about this vitamin.

VITAMIN D

Vitamin D activity is exhibited by ten oil-soluble sterols. The two most important are: (a) D₂, *viosterol* or activated ergosterol. When ergosterol, the sterol of fungi and yeast, is irradiated with ultraviolet light, it is transformed into D₂. (b) D₃, *activated dehydrocholesterol*; this is the principal form of vitamin D in fish oils. It is produced in the skin, fur or feathers of animals exposed to sunlight or ultraviolet light at 2600 to 3000 Angstrom units with a maximum at 2804 Å. In winter and in smoky cities the efficient rays of the sunlight have been completely filtered out. D₃ is also produced in irradiated milk.

vitamin D. Wright²⁸ expresses the present-day feeling that vitamin D is a helpful adjunct in the treatment of acne but is not curative when given alone.

Pemphigus Vulgaris.—Strangely enough, in the treatment of pemphigus vulgaris where the rationale is the weakest, some satisfactory results have been recorded. Ludy³⁰ reported six patients successfully treated with large doses of viosterol. Tauber and Clarke³¹ reported nine patients so treated. Eight of these showed great alleviation, although three died later of intercurrent diseases. In our hands 300,000 to 400,000 units of vitamin D daily has produced remissions in some of the cases of pemphigus vulgaris. The improvement, however, is only temporary and vitamin D is rarely of any value in the succeeding exacerbation. In no case has it produced a cure. It is valuable, however, as one of the modalities which may produce a remission in this fatal disease.

Scleroderma.—Cornbleet and Struck³² treated eleven cases of scleroderma over a period of nine months with 200,000 to 300,000 units of vitamin D daily with satisfactory results. However, it is our feeling that equally satisfactory results can be obtained with less expensive methods.

X-ray Burns.—The treatment of x-ray burns with an ointment of cod liver oil and white wax has been suggested by Dr. James H. Mitchell of Chicago. We have found this satisfactory in allaying pain and stimulating healing.

The use of vitamins therapeutically is in a state of flux. Much more clinical experience is necessary.

BIBLIOGRAPHY

1. Proceedings of the Institute of Medicine of Chicago, 15: 198, 1940.
2. Popper: Arch. Path., 51: 1, 1941.
3. Frazier and Hu: Arch. Int. Med., 48: 507, 1931.
4. Lowenthal: Arch. Derm. & Syphil., 28: 700, 1933.
5. Lehman and Rappaport: J.A.M.A., 114: 386, 1940.
6. Brunsting, L. C.: Arch. Dermat. & Syphil., 43: 42, 1941.
7. Gross: Arch. Dermat. & Syphil., 45: 504, 1941.
8. Peck, Chargin and Sobotka: Arch. Dermat. & Syphil., 43: 223, 1941.
9. Durand, Spickard and Burgess: J. Pediat., 14: 74, 1939.
10. Madden: J.A.M.A., 115: 588, 1940.
11. Sutton and Ashworth: J. Lab. & Clin. Med., 25: 1188, 1940.
12. Lynch: Arch. Derm. & Syphil., 42: 491, 1940.
13. Kühman: Klin. Woch., 18: 1117, 1939.

exposure to summer sunlight. It was assumed such improvement might be due to increased production of vitamin D in the skin; hence, its use is suggested in these disorders. While it is true that the detailed chemistry of calcium in cellular physiology is imperfectly understood, there is evidence of a disturbance of calcium balance in *scleroderma*. Vitamin D stabilizes calcium balance; hence, its use was suggested in this disorder.

Arthritis.—Very large doses of vitamin D (massive dose therapy, 300,000 to 400,000 units daily) were first used in the treatment of arthritis, apparently without any marked effect on serum calcium or phosphorus levels, and without any appreciable effect on the calcium in the bones. Certain unpleasant reactions, such as nausea, gastric upsets, headaches and frequency of urination, occasionally occurred.

Psoriasis.—Cedar and Zon²⁶ first used these large doses of vitamin D in fifteen cases of psoriasis; in eleven involution occurred in six to twelve weeks but in six of these recurrence was noted shortly afterward. George Clark²⁷ reported a joint study of the Cincinnati Dermatological Society using large doses of vitamin D in 144 cases of psoriasis during the winter months. He found the method less satisfactory than other methods in use in former years. Wright²⁸ concluded that the method is inadvisable in psoriasis due to a lack of specificity, high cost and impermanence of results. Madden²⁹ even considered the method positively dangerous.

Wright in his paper calls attention to one case of *pustular psoriasis*, a condition which is notoriously recalcitrant to treatment, that responded to high vitamin D therapy. We also have had some favorable results in pustular psoriasis and would recommend the method. Ampoules containing 25,000 units of vitamin D, either alone or in combination with vitamin A, are on the market.

Acne Vulgaris.—This is another chronic, resistant skin disorder in which it is difficult to evaluate new methods of therapy. Long periods of observation and a large number of patients are necessary due to the frequency of spontaneous exacerbations and remissions. Several papers have appeared recently on the treatment of acne vulgaris with high doses of

SPECIFIC SKIN INFECTIONS: CUTANEOUS SYPHILIS AND TUBERCULOSIS

S. WILLIAM BECKER, M.D.*

CUTANEOUS SYPHILIS

THE cutaneous manifestations of syphilis¹ may be divided into those of the early stages (the primary lesion of chancre, secondary and recurrent secondary syphilids) and those of the late stage (tertiary syphilids).

Early Cutaneous Syphilis

Primary Lesion

The primary lesion, or *chancre*, starts as an erythematous macule which becomes an indurated, eroded papule occurring at the site of inoculation and varying in appearance with the location. On the external female genitalia it is usually quite small, is larger on the male genitalia and still larger in other locations, such as the lip. Owing to secondary infection, a chancre may become ulcerated. A chancre of the *cervix uteri* usually consists of a boggy induration, with or without erosion. A few days after the appearance of the chancre, a lymph node in the group draining the region of inoculation enlarges in the form of a solitary, nontender, painless swelling (the satellite bubo). The adenopathy accompanying a chancre on the *cervix uteri* is in the internal iliac group and is not noted by the patient or physician. This feature probably accounts for the frequent failure to discover infection in women in its early stage.

CASE I.—Miss D. K., aged twenty-three, presented a painless, nontender, indurated, eroded nodule on the lower lip (Fig. 5) which had been present for five weeks. It was covered by a sero-

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14. Vilter, Ering and Spies: J.A.M.A., 115: 209, 1940.
15. Gross, Paul: Arch. Derm. & Syphil., 43: 504, 1941.
16. Crandon, Lund and Dill: New Eng. J. Med., 223: 353, 1940.
17. Sulzberger and Oser: Proc. Soc. Exper. Biol. & Med., 32: 716, 1935.
18. Chapman and Morrell: Proc. Exper. Biol. & Med., 32: 813, 1935.
19. MacDonald and Johnson: Arch. Derm. & Syph., 43: 682, 1941.
20. Cornbleet: Arch. Derm. & Syphil., 35: 471, 1937.
21. Morowitz: Klin. Woch., 13: 324, 1934.
22. Szent-Györgyi *et al.*: Deutsch. med. Wchnschr., 62: 1325, 1936.
23. Kugelmass: J.A.M.A., 115: 519, 1940.
24. Goldfarb: Arch. Derm. & Syphil., 43: 536, 1941.
25. Scarborough: Lancet, 2: 611, 1940.
26. Cedar and Zon: Public Health Reports, 52: 1580, 1937.
27. George Clark: Arch. Derm. & Syphil., 41: 664, 1940.
28. Wright: Arch. Derm. & Syphil., 43: 145, 1941.
29. Madden: J.A.M.A., 141: 664, 1940.
30. Ludy: Urol. & Cut. Rev., 36: 817, 1932.
31. Tauber and Clarke: Arch. Derm. & Syphil., 40: 82, 1939.
32. Cornbleet and Struck: Arch. Derm. & Syphil., 35: 188, 1937.

ally seen in individuals in poor physical condition, and leave superficial scars after involution.

CASE II.—N. M., aged twenty-four, presented a generalized maculopapular eruption involving the entire cutaneous surface (Fig. 6), including that of the palms and soles, which had been present for ten days. There were some moist papules on the

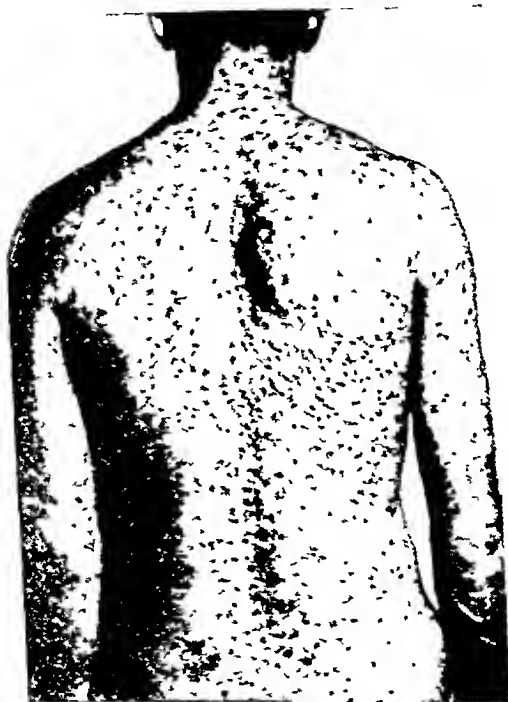


Fig 6 (Case II).—Maculopapular syphilid, the commonest eruption of secondary syphilis. (Finnerud in *MEDICAL CLINICS OF NORTH AMERICA*, Nov., 1931.)

genitalia and about the anus and erosions on the right buccal mucosa and the left tonsil. The Kolmer reaction of the blood serum was 4+ and the Kahn reaction was 4 plus. Diagnosis was made of maculopapular secondary syphilid.

Recurrent Secondary Lesions

From several months to two or three years after the disappearance of the secondary eruption recurrent secondary

sanguineous crust. Darkfield examination showed *Spirochaeta pallida*. The Kolmer reaction of the blood serum was 4-4 and the Kahn was 4 plus. Diagnosis was made of primary syphilis.



Fig. 5 (Case I).—Chancre of the lower lip. (Becker and Obermayer, "Modern Dermatology and Syphilology," J. B. Lippincott Co., publisher.)

Secondary Lesions

About eight weeks after the appearance of the chancre a generalized eruption usually appears, which varies from the macular variety (*roseola*), through the more common maculopapular and papular to the less common pustular, ecthymatous and rupial varieties. *Roseola* consists of numerous, closely set macules, varying from a few millimeters to a centimeter in diameter. At first their color is pink, but they become darker in a few days and show the characteristic raw tan or copper color. The eruption is differentiated from toxic erythema by the regularity of distribution and darker color. *Maculopapular syphilid* is composed of slightly elevated, indurated maculopapules, at first pale pink, later becoming darker. *Papular syphilids* vary greatly in appearance, depending on the nature of the individual papules. The elements may be small or large, may have a follicular location, and may be grouped. *Pustular, impetiginous* and *rupial syphilids* are composed of pustular or crusted elements, are usu-

Darkfield examination of the scrotal lesions showed a large number of *Spirochaeta pallida*, the Kolmer reaction of the blood serum was 4-4 and the Kahn reaction was 4 plus, the spinal fluid was negative, and diagnosis was made of recurrent secondary syphilids constituting a cutaneous relapse. The relapse was probably caused by treatment of insufficient duration and of inferior quality (neoarsphenamine alone rather than combined bismuth and neoarsphenamine).

Treatment was instituted by means of combined bismuth and arsenical but the lesions extended peripherally and became annular (Fig. 7). At this time he developed mucous patches in the throat. Since routine treatment did not control the process, non-specific therapy was instituted in the form of autohemetic injections twice weekly, and daily generalized exposure to ultraviolet light, along with double doses of bismuth subsalicylate twice weekly. After one month of this combined specific and non-specific therapy the lesions on the scrotum and in the throat had healed. Routine treatment for early syphilis was then instituted. After seven months the blood test became negative.

Diagnosis of Early Syphilis

The diagnosis of early syphilis is made by laboratory rather than clinical methods. Darkfield examination of material from the lesions for *Spirochaeta pallida* and examination of the blood by the complement-fixation and/or flocculation reactions are the only completely reliable methods. The blood test will become positive after a chancre has been present for eight weeks, provided that the patient has not been given local or systemic treatment.

Late Cutaneous Syphilis

The criteria for *diagnosis* of late syphilids are the time of appearance (ordinarily five or more years after infection) and their morphologic characteristics. The prolonged presence of spirochetes in the body has resulted in the production of an allergic state in the tissues, consequently the process is destructive. The degree of allergy varies greatly: if slight, small nodular elements may heal with resulting scarcely perceptible atrophy; if pronounced, violent tissue reaction may result in large lesions, extensive destruction and subsequent

lesions may appear, which tend to be more localized, especially about the genitalia, on the oral mucosa and on the palms and soles. Those in the mouth (*mucous patches*) and about the genitalia (*condylomata lata*) soon become eroded and are highly infectious. They are in areas involved in intimate physical contact, and are responsible for much of the transmission of the disease.



Fig. 7 (Case III).—Recurrent annular papules on scrotum. (Becker and Obermayer, "Modern Dermatology and Syphilology," J. B. Lippincott Co., publisher.)

CASE III.—Mr. M. H., aged twenty-eight, presented indurated button-like eroded papules on the scrotum. He had been treated seven months previously for primary syphilis by means of neoarsphenamine twice weekly for seven weeks. No bismuth or mercury had been given. After this treatment the blood test had been reported negative and treatment had been discontinued.

Darkfield examination of the scrotal lesions showed a large number of *Spirochaeta pallida*. the Kolmer reaction of the blood serum was 4-4 and the Kahn reaction was 4 plus, the spinal fluid was negative, and diagnosis was made of recurrent secondary syphilids constituting a cutaneous relapse. The relapse was probably caused by treatment of insufficient duration and of inferior quality (nearsphenamine alone rather than combined bismuth and nearsphenamine).

Treatment was instituted by means of combined bismuth and arsenical but the lesions extended peripherally and became annular (Fig. 7). At this time he developed mucous patches in the throat. Since routine treatment did not control the process, non-specific therapy was instituted in the form of autohemic injections twice weekly, and daily generalized exposure to ultraviolet light, along with double doses of bismuth subsalicylate twice weekly. After one month of this combined specific and non-specific therapy the lesions on the scrotum and in the throat had healed. Routine treatment for early syphilis was then instituted. After seven months the blood test became negative.

Diagnosis of Early Syphilis

The diagnosis of early syphilis is made by laboratory rather than clinical methods. Darkfield examination of material from the lesions for *Spirochaeta pallida* and examination of the blood by the complement-fixation and/or flocculation reactions are the only completely reliable methods. The blood test will become positive after a chancre has been present for eight weeks, provided that the patient has not been given local or systemic treatment.

Late Cutaneous Syphilis

The criteria for *diagnosis* of late syphilids are the time of appearance (ordinarily five or more years after infection) and their morphologic characteristics. The prolonged presence of spirochetes in the body has resulted in the production of an allergic state in the tissues, consequently the process is destructive. The degree of allergy varies greatly: if slight, small nodular elements may heal with resulting scarcely perceptible atrophy; if pronounced, violent tissue reaction may result in large lesions, extensive destruction and subsequent

healing with tissue defect, as in Case IV. The ten criteria for the diagnosis of late syphilids are: solitariness; asymmetry; indolence; induration; arciform configuration; punched-out borders of ulcers; tissue destruction; central healing and peripheral extension; formation of atrophic, noncontractile scars; and peripheral hyperpigmentation about the scars.



A

B

Fig. 8 (Case IV).—*A*, Multiple gummata of leg; *B*, solitary gumma, extending deeply, on forearm in same patient. (Becker and Obermayer, "Modern Dermatology and Syphilology," J. B. Lippincott Co., publishers.)

CASE IV.—Mrs. L. P., aged twenty-eight, presented indolent ulcers which had appeared on the left leg two and a half years previously following a bruise, and on the right arm for one month following a "bump" (Fig. 8). The lesions on the leg spread

peripherally, leaving an atrophic, noncontractile scar with peripheral hyperpigmentation. The Kolmer reaction of the blood serum was 4-4 and the Kahn was 2 plus. Spinal fluid was negative on examination. Diagnosis was made of gummatous late syphilis.

Treatment of Syphilis

Chemotherapy

Treatment of syphilis is purely systemic. Local therapy to syphilitic cutaneous lesions has negligible results.

Early Syphilis.—The principles of therapy for early syphilis are: *more arsphenamines*, relatively *less bismuth*, and *no rest periods for one year* (Table 1). My impression that the concurrent administration of arsenicals and bismuth gives better therapeutic results with less tendency to complications has been given experimental support by Clausen, Tatum and Longley,² who found that, while therapeutic effects of arsenicals and bismuth are additive, the toxic effects are not additive, so that better therapeutic results may be obtained with lessened toxicity by combining the two types of drugs. Treatment in the chancre stage may be carried out routinely according to the method given in Table 1, unless some other systemic disease contraindicates.

Secondary Stages.—Treatment of syphilis in the stage of disseminated secondary eruption or in the recurrent secondary period should be initiated by the use of *soluble bismuth* for two weeks, after which the treatment is carried out according to Table 1, starting at the tenth day, with the dose of the first injection somewhat reduced.

Late Syphilis.—The principles of therapy for late syphilis are: *less arsphenamine*, relatively *more bismuth*, and *iodides* in most cases. Treatment of syphilis in the late stages is carried out according to the baseline schedule given in Table 2, with alterations in case the viscera show clinical involvement.

Nonspecific Therapy

It is sometimes found that chemotherapeutic measures are not sufficient to control the syphilitic process. This failure occurs only rarely in the early stages, but more frequently in the late period of the disease. In such event, it is customary

TABLE 1
TREATMENT FOR ASYMPTOMATIC EARLY SYPHILIS

Days	Neoarsphen- amine, Gm.	Bismuth Salicylate, Cc.	Days	Neoarsphen- amine, Gm.	Bismuth Salicylate, Cc.
1	0.45	.	184	0.6	1.0
3	0.9	.	189	0.6	1.0
5	0.9	..	194	0.6	1.0
10	0.6	1.0	199	0.6	1.0
15	0.6	1.0	204	0.6	1.0
20	0.6	1.0	209	0.6	1.0
25	0.6	1.0	214	0.6	1.0
30	0.6	1.0	221	2.0
35	0.6	1.0	228		2.0
40	0.6	1.0	235		2.0
45	0.6	1.0	242		2.0
50	0.6	1.0	249		2.0
55	0.6	1.0	256	0.45	1.0
60	0.6	1.0	261	0.6	1.0
67	..	2.0	266	0.6	1.0
74	..	2.0	271	0.6	1.0
81	..	2.0	276	0.6	1.0
88	..	2.0	281	0.6	1.0
95	..	2.0	286	0.6	1.0
102	0.45	1.0	291	0.6	1.0
107	0.6	1.0	298	..	2.0
112	0.6	1.0	305		2.0
117	0.6	1.0	312		2.0
122	0.6	1.0	319		2.0
127	0.6	1.0	326		2.0
132	0.6	1.0	333	0.45	1.0
137	0.6	1.0	338	0.6	1.0
144		2.0	343	0.6	1.0
151		2.0	348	0.6	1.0
158		2.0	353	0.6	1.0
165		2.0	358	0.6	1.0
172		2.0	363	0.6	1.0
179	0.45	1.0	368	0.6	1.0

Examination of spinal fluid.

One month rest.

Ten bismuth salicylate at weekly intervals.

Three months rest.

Ten bismuth salicylate.

Six months rest.

Ten bismuth salicylate.

One year rest.

Ten bismuth salicylate.

Life-time observation.

This schedule is for a healthy adult male, and the dosage of neoarsphenamine should be slightly smaller for women. The bismuth dosage may remain the same.

Mapharsen may be substituted for neoarsphenamine in a dose of 0.03 Gm. to 0.6 Gm.

TABLE 2

TREATMENT FOR UNCOMPLICATED LATE SYPHILIS

Days	Neoarsphen- amine, Gm.	Bismuth Salicylate, Cc.	Days	Neoarsphen- amine, Gm.	Bismuth Salicylate Cc.
1 to 70		10 weekly injections, 1.0 to 2.0 cc.	1 month rest		
71	0.45	1.0	292 to 352		8 weekly in- jections, 1.0 to 2.0 cc.
76	0.6	1.0	1 month rest		
81	0.6	1.0	382	0.45	1.0
86	0.6	1.0	387	0.6	1.0
91	0.6	1.0	392	0.6	1.0
96	0.6	1.0	397	0.6	1.0
101	0.6	1.0	402	0.6	1.0
106	0.6	1.0	407	0.6	1.0
1 month rest			412	0.6	1.0
136 to 196		8 weekly in- jections, 1.0 to 2.0 cc.	417	0.6	1.0
1 month rest			3 months rest		
226	0.45	1.0			10 weekly injections, 1.0 to 2.0 cc.
231	0.6	1.0	6 months rest		
236	0.6	1.0			10 weekly in- jections.
241	0.6	1.0	1 year rest		
246	0.6	1.0			10 weekly in- jections.
251	0.6	1.0			
256	0.6	1.0			
261	0.6	1.0			

If blood test negative, place on observation. If positive, give one course of bismuth each year.

Iodides may be given throughout.

This schedule is for a healthy adult male, and the dosage of neoarsphenamine should be slightly smaller for women. The bismuth dosage may remain the same.

Mapharsen may be substituted for neoarsphenamine in a dose of 0.03 Gm. to 0.06 Gm.

to employ nonspecific measures, either alternated or combined with chemotherapeutic measures. During the early period of the disease, it is the relapsing manifestation or the destructive process (premature tertiarism) which necessitates

change in treatment. Such a change was made in the treatment already enumerated in connection with Case III. In this instance, daily *ultraviolet exposures* and *autohemic injections* were combined with double doses of bismuth. *Rest* and *sunshine* are important measures in late syphilis.

Hyperpyrexia.—The most common form of nonspecific treatment in use at the present time is that producing hyperpyrexia. The most convenient and safest method consists in the use of typhoid vaccine, injected intravenously every second day. Care should be taken to make sure the material has been prepared for intravenous use. Other methods of fever therapy consist in inoculation with tertian malaria, and the use of various mechanical and electrical devices.

Milder nonspecific effects may be obtained by injection of foreign protein substances or the use of autohemic injections. Nonspecific measures should be used for only a few weeks and are preferably combined with specific measures.

Prognosis in Syphilis

Can syphilis be cured? In a small series of fifty-five patients with early syphilis treated at the University of Chicago Clinics for two or more years by the aforementioned method. Walsh and I³ found that the patients were clinically cured (negative blood and spinal fluid reactions and negative physical examination) in all instances. In late syphilis, on the other hand, it is customary to speak of "arrest" rather than "cure." It is evidently possible to arrest the active disease process in all cases, but the functional result will depend on the amount of damage that has already resulted.

CUTANEOUS TUBERCULOSIS

Cutaneous tuberculosis¹ may be divided into two types, tuberculosis proper and tuberculids; the latter are allergic reactions. The three main varieties of the former are lupus vulgaris, tuberculosis verrucosa cutis and scrofuloderma (tuberculosis colliquativa). A less usual variety is primary inoculation tuberculosis. Among the latter are papulonecrotic tuberculids and nodulonecrotic tuberculids including erythema induratum, and lichen scrofulosorum.

Lupus Vulgaris

Lupus vulgaris occurs predominantly about the face and is characterized by the presence of small brownish nodules, which show the so-called "apple-jelly" color on diascopic pressure. The condition spreads slowly, with central healing. The central scar, which tends to be contractile, often shows recurrent nodules, a feature never found in the scars of late syphilids.

CASE V.—Mrs. L. J., aged sixty-two, presented a plaque on the left side of the neck (Fig. 9) of fourteen years' duration. Since the age of sixteen she had had a small subcutaneous nodule in this

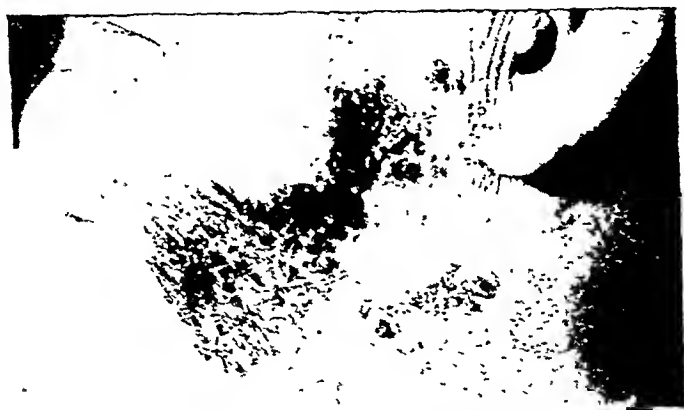


Fig. 9 (Case V).—Lupus vulgaris. (Becker and Obermayer, "Modern Dermatology and Syphilology," J. B. Lippincott Co., publisher.)

region which was occasionally slightly tender but had never suppurated. At the age of forty-eight a purplish-red plaque appeared on the skin which had extended peripherally. It had been treated by various measures, including local treatment by the Finsen lamp. The periphery of the plaque was studded with brownish nodules which showed typical apple-jelly color on diascopic pressure. The center of the plaque consisted of a scar in which the typical nodules could also be seen. Diagnosis was made of lupus vulgaris. The tuberculin test with old tuberculin was positive in a dilution of 1:1,000,000.

Scrofuloderma

Scrofuloderma results from the spread of deep tuberculous infection (bones, joints, lymph nodes, subcutaneous tissue) to the skin as the result of suppuration with subsequent ulceration.



Fig. 10. (Case VI).—Scrofuloderma. Bilateral cervical lymphadenitis with unilateral suppuration and involvement of the skin. (Becker and Obermayer, "Modern Dermatology and Syphilology," J. B. Lippincott Co., publisher.)

CASE VI.—Master H. M., a Mexican, aged six, presented a draining mass in the right submaxillary region (Fig. 10). The mass had been present for two years but had been draining for

only two weeks. Diagnosis was made of tuberculosis colliquativa (scrofuloderma), verified by biopsy. He also showed grouped follicular lesions on the trunk which constituted lichen scrofulosorum, a tuberculid, also verified by biopsy.

Tuberculosis Verrucosa Cutis

Tuberculosis verrucosa cutis is the most common variety of *inoculation tuberculosis*. It starts at the site of inoculation as a small verrucous lesion which enlarges and either forms a large verrucous plaque or, as the result of central healing, produces

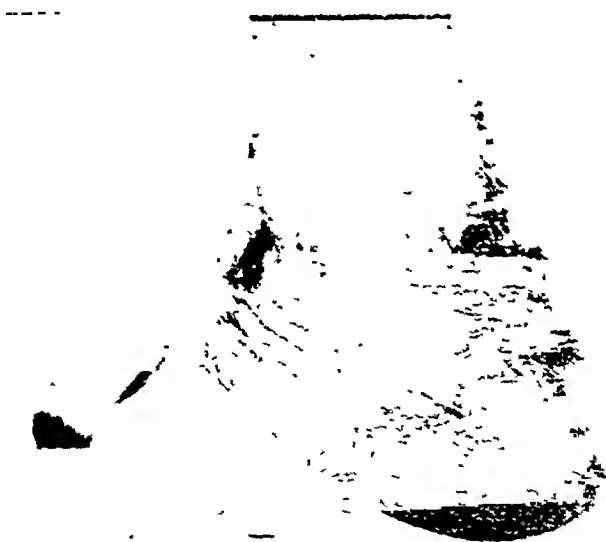


Fig. 11 (Case VII).—Tuberculosis cutis verrucosa of heel, with scar from previous tuberculous sinus.

an annular verrucous lesion with central scar. The condition must be differentiated from verrucous or vegetative pyoderma, and blastomycosis, which ordinarily presents a moister plaque with peripheral abscesses, in the pus from which blastomyces can usually be demonstrated. Microscopic examination may be necessary for differentiation.

CASE VII.—Mr. W. Y. K., Chinese, aged twenty-seven, developed a fluctuant swelling just below the right internal malleolus. The abscess was opened and tuberculosis was diagnosed by

biopsy and animal inoculation. The lesion eventually healed, and he was seen four years later with a verrucous lesion just over the right tendo Achilles just above the heel (Fig. 11), which had been present for eight months. There had been no subjective sensations. Diagnosis was made of tuberculosis verrucosa cutis, which was verified by biopsy. Examination of the lungs by roentgenogram showed no abnormalities. The lesion was treated by electrocautery.



Fig. 12 (Case VIII).—Inoculation tuberculosis. The lesion on the heel followed trauma. The two tumors are enlarged lymph nodes in the femoral region, one of which has broken down.

Primary Inoculation Tuberculosis

Primary inoculation tuberculosis most often occurs in childhood, since adults usually are infected with tuberculosis. The primary lesion or tuberculous chancre is usually a crusted ulcer by the time it is first seen. Occasionally it is so insignificant that it is not discovered until the adenopathy points the finger of suspicion to inoculation tuberculosis and the lesion is discovered in an obscure location, such as between the toes. The regional lymph nodes enlarge and tend to suppurate.

CASE VIII.—Master E. M., aged four, presented a callus on the right foot which had been present for three months. Pus could

be expressed from the lesion on pressure. Two or three weeks later erythematous streaks were noted on the leg associated with swelling of a lymph node in the femoral area (Fig. 12). Diagnosis was made of primary inoculation tuberculosis which was verified by biopsy. Microscopic examination of an involved inguinal lymph node showed tuberculous lymphadenitis.

Tuberculids

As a result of alteration of tissue reaction, in that it has become allergic, a more violent reaction to the tubercle bacilli and their products takes place, resulting in tissue destruction. Hence, most of the various types of tuberculids are necrotic lesions. The chief exception is the follicular variety (*lichen scrofulosorum*) which is characterized by grouped follicular papules in a disseminated eruption. Tuberculids are symmetrically distributed, in contrast to late syphilids which are usually asymmetrical. The papulonecrotic tuberculids and their resulting scars are usually seen on the extensor surfaces of the elbows and knees. The nodulonecrotic variety is seen on the legs. A particular variety, with lesions localized on the lower calves, is known as *erythema induratum*. Papulonecrotic lesions on the face constitute *acnitis* and those on the hands are known as *folliclis*.

CASE IX.—Miss A. F., aged forty-two, presented papulonecrotic lesions and scars over the extensor surfaces of the arms (Fig. 13) and legs which had appeared in crops for many years. She had had swelling of the cervical lymph nodes each spring for several years and twelve years ago she had had some lymph nodes removed. The nodes had never suppurated and the skin over them had never broken down. At sporadic intervals she had had slight puffiness involving one or more of the extremities. A year ago the left wrist had been involved. Diagnosis was made of papulonecrotic tuberculids.

CASE X.—Mrs. E. S., aged forty-nine, presented multiple ulcers and scars on both legs (Fig. 14) which had been present for three years. The lesions had started as subcutaneous erythematous nodules, some of which had softened, ulcerated and healed, leaving atrophic, noncontractile scars. Tuberculin test with old tuberculin was negative in a dilution of 1:1,000,000, but positive in a

dilution of 1:100,000. Diagnosis was made of nodulonecrotic tuberculid.



Fig. 13 (Case IX).—Papulonecrotic tuberculids. Recent lesions are crusted and atrophic noncontractile scars about the elbow are the sites of previous lesions. (Becker and Obermayer, "Modern Dermatology and Syphilology," J. B. Lippincott Co., publisher.)

Treatment and Prognosis of Cutaneous Tuberculosis

Treatment of tuberculosis is both systemic and local, with different emphasis on each phase in the different varieties.

Systemic Measures

Systemic measures are of the greatest importance and consist of rest, relaxation, daily generalized ultraviolet irradiation (if the patient does not have active pulmonary tubercu-



Fig. 14 (Case X).—Nodulonecrotic tuberculids. The bilateral distribution, together with lack of characteristics for lesions of late syphilis, distinguishes the condition from the latter. (Becker and Obermayer, "Modern Dermatology and Syphilology," J. B. Lippincott Co., publisher.)

losis), high caloric diet, and intravenous injections of sodium gold thiosulfate or mapharsen. Foci of infection should be removed in patients with tuberculids.

Local Measures

Local treatment varies with the type of tuberculosis. *Lupus vulgaris* is best treated by means of deep surgical excision or electrocoagulation. Intensive local ultraviolet therapy is useful, as is injection of a 15 per cent suspension of Starch, U.S.P. *Tuberculosis verrucosa cutis* should be excised surgically or destroyed by surgical diathermy. *Scrofuloderma* is treated by filtered roentgen rays. Intensive local infra-red therapy is useful. If the lesion is fluctuant, the pus may be aspirated and 10 per cent iodoform in glycerin injected into the cavity. Removal or destructive treatment of the primary lesion in *inoculation tuberculosis* is a prime necessity, to be followed by removal or treatment of the infected lymph nodes. Intensive ultraviolet irradiation is also useful in *erythema induratum*.

Prognosis

The results of therapy for cutaneous tuberculosis depend largely on the fidelity with which the patient carries out general measures. The prognosis should always be guarded, since recurrences are the rule in most varieties of the disease.

BIBLIOGRAPHY

1. Becker, S. W. and Obermayer, M. E.: *Modern Dermatology and Syphilology*. J. B. Lippincott Company, Philadelphia, 1940.
2. Clausen, N. M., Tatum, A. L. and Longley, B. J.: Personal communication.
3. Walsh, E. N. and Becker, S. W.: The Use of Bismuth Compounds in Syphilotherapy. *J.A.M.A.*, 116: 484 (Feb. 8) 1941.

PYOGENIC INFECTIONS OF THE SKIN

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PYOGENIC infections of the skin are among those most frequently encountered by the practitioner and present a definite therapeutic problem as evidenced by the constant introduction of new methods of treatment.

Staphylococci and streptococci of various types are present on the normal skin but only in specific instances become pathogenic and give rise to distinctive lesions of the skin. Their entrance into the integument is probably through the minute orifices of the hair follicles and sweat glands, or through abrasions in the skin, and is facilitated by friction, maceration with sweat, soiled clothing and underwear, lack of bathing and improper hygiene which produces a lowered resistance to the omnipresent cocci. Infection is, therefore, in most instances of superficial exogenous origin, although pyodermas may be secondary to other dermatoses, particularly the pruritic forms of eczema, infectious eczematoid dermatitis, exfoliative dermatitis, scabies, pediculosis and the like. That systemic factors frequently play a role is indicated by the occasional finding of a hyperglycemia in instances of furunculosis, frank diabetes and carbuncle, and by high blood urea counts and varying degrees of anemia and cachexia that may be noted in severe pyodermas.

In the group of disorders under discussion, comprising the pyodermas, are included the impetigo contagiosa of Tilbury Fox, the closely related echthyma, the impetigo of Bockhart, the different varieties of folliculitis, erysipelas due to a specific streptococcus, furuncles and carbuncles, the less common axillary hydradenitis—a sweat-gland abscess of staphylococcic origin, and certain rare pustular eruptions of

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the skin. In this communication we shall attempt a comparative evaluation of modern methods of treatment rather than a detailed clinical description of banal lesions, the diagnosis of which is self-evident in most instances even to the layman.

*IMPETIGO CONTAGIOSA

Impetigo contagiosa is one of the commonest skin disorders—a contagious, auto-inoculable, pyogenic infection caused mainly by a streptococcus. According to some recent authors (Epstein and Tachau) it may be caused in some cases by a staphylococcus. The incubation period is probably not over a few hours or a few days.



Fig. 15.—Impetigo contagiosa.

The earliest lesions are thin-walled superficial vesicles which rapidly form yellowish, "stuck-on" gummy crusts, on the removal of which superficially denuded red spots are evident (Fig. 15). The lesions multiply rapidly, are found most frequently on the face and neck, spread to the scalp and hands, and in unusual instances are disseminated over the trunk. They show a tendency toward confluence, may as-



Fig. 16.—*Impetigo circinata*.



Fig. 17.—*Impetigo of the lips*.

sume a circinate form (*impetigo circinata*, Fig. 16), or become bullous (*impetigo bullosa*). Systemic symptoms are conspicuously absent although enlarged cervical glands may be found. In rare instances a nephritis occurs. Involvement of the vermilion border of the lips is not infrequent (Fig. 17).

A more severe variety of the disease is the staphylococcic impetigo of the newborn and young infants, known as *pemphigus neonatorum* or *pemphigoid*, in which there is a definite mortality and which may eventuate in an exfoliative dermatitis. The management of this particular form of impetigo will not be considered in this clinic.

The ordinary impetigo of older children and adults (often called "barber's itch") is easily recognized, although in exceptional cases it may simulate herpes, *tinea circinata* or acute eczema.

Treatment

The treatment of impetigo is a simple office procedure and should be undertaken promptly without waiting for a bacteriologic study to determine whether a streptococcus or a staphylococcus is the invading organism. even though Epstein feels that a differentiation of a staphylococcus impetigo has some therapeutic significance. In our experience in a fairly large number of cases we have not encountered any difference among the various types in their responses to treatment.

The routine of therapy which we have followed with only slight variation is as follows: On the first visit to the office the lesions are sponged with *peroxide* and the crusts gently removed with forceps. The base of the lesions is then touched lightly with a 2 per cent solution of *iodine* in chemically pure benzol. The different areas are now exposed to the unfiltered rays of the water-cooled *Kromayer lamp* for one or two minutes, a suberythema dose being administered. For home use the patient is given a prescription for a saturated solution of *boric acid* with the addition of 25 per cent *merthiolate* (1:1000) and an ointment or paste with a suitable base, containing 5 per cent *boric acid*, 5 per cent *ammoniated mercury*, and 3 per cent *sulphonated bitumen*. The instructions are to

apply the solution after soaking off any remaining crusts with soap and water, and after drying to cover the lesions with the ointment twice daily. The office treatments are repeated on the third and fifth days and a cure is obtained on the average in five to seven days. We have found the above outlined therapy to be more effective than use of the official 10 per cent ammoniated mercury ointment, which often produces a mercurial dermatitis.

In the literature will be found of course many other methods of topical treatment. Sulzberger for instance advises, in cases that are intolerant to mercury, either the *quinolor ointment* of Squibb or *Benzox ointment*. Two per cent aqueous *gentian violet* is recommended by some but, as has recently been pointed out, it may cause superficial ulceration. *Silver nitrate* (5 to 10 per cent), although effective, produces disfiguring black spots. *Colloidal mercury ointment* has recently been advocated. *Wyeth's alulotion*, a colloidal Kaolin lotion containing ammoniated mercury, is said to cure impetigo on the average in seventeen days. Even more recently *sulfanilamide* in a topical form has been advocated in the treatment of impetigo and ecthyma. Brunsting used a 4 per cent sulfanilamide ointment in impetigo. Sams and Coplund found *sulfathiazole powder* or 5 to 20 per cent concentration of sulfathiazole in cod liver oil ointment curative in various pyodermas. Lain advocated sulfanilamide (4 to 8 gm.) in glycerin (1 ounce) in similar cases. Toxic effects from the local use of sulfanilamide have not been observed except an occasional dermatitis. The internal administration of sulfanilamide preparations in a disease as readily cured as impetigo should not receive serious consideration.

IMPETIGO OF BOCKHART

This is a pin-head sized follicular pustular eruption occurring mainly on the extremities (Fig. 18) usually secondary to a discharging wound, sinus or furuncle. It is fairly common in children and in unkempt adults, and is rarely associated with mild degrees of fever and a regional adenitis. It is best treated with local antiseptics similar to those used in impetigo, plus disinfecting baths with permanganate solution.

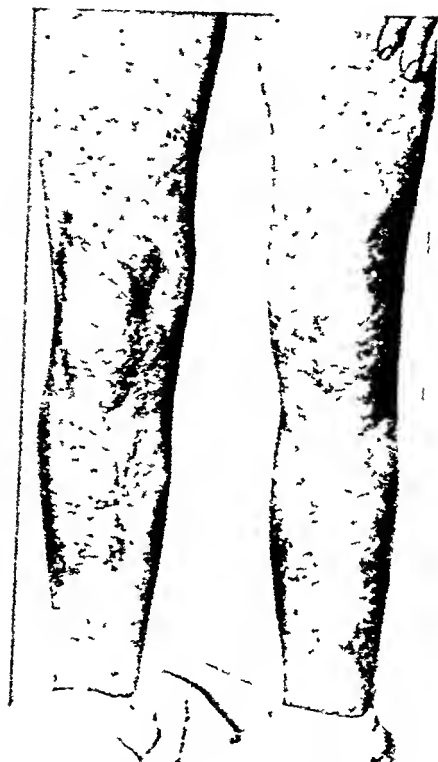


Fig 18—Impetigo of Bockhart.

ECTHYMA

Ecthyma is to be looked upon as a more deep-seated form of impetigo of streptococcic origin, producing flat crusted lesions with an inflammatory areola (Fig. 19). Superficial ulceration is frequently found underneath the crust. We have found these cases much more resistant to local treatment than ordinary impetigo, but the general principles of local therapy are identical—cleanliness, sunshine and ultraviolet light are useful adjuvants to treatment. Scars may remain when healing takes place. The etiologic factor is a hemolytic streptococcus, occasionally a staphylococcus, with trauma as a factor. In a recent case, *sulfanilamide* in adequate doses by mouth produced a rapid cure.



Fig. 19.—Ecthyma.

ERYSIPELAS

Erysipelas is a specific streptococcic infection of the lymphatic spaces of the skin, running a febrile course and characterized by rapid spreading and migration. The tense, elevated, edematous advancing border of the lesions, at times studded with vesicles or bullae, should readily differentiate the eruption from an acute eczematous dermatitis, which it at times resembles. The infection is most common on the face and frequently produces edema of the soft tissues about the eyelids and in rare instances may result in local gangrene.

Constitutional symptoms vary in their severity but are most marked in the young and in elderly debilitated and alcoholic patients suffering from chronic disease. The temperature may be elevated to 102° F. or 103° F. or higher and is

accompanied by chills, sore throat, rapid pulse, delirium and other evidences of toxemia. Milder cases are relatively afebrile. Serious *complications* are cellulitis, subcutaneous abscesses, broncho-pulmonary conditions, nephritis, hepatitis, meningitis and cardiac dilatation. The disease is rarely self-limited and may last several weeks.

The infecting organism enters the skin through a traumatic abrasion or a fissure. The ear and nose are frequent points of origin, a chronic eczema with fissuring being noted, or an associated rhinitis or discharging ear. On the feet the fissures between the toes from an epidermophyton infection are the atria of infection. Surgical erysipelas following operative procedures is rarely seen in the present era of asepsis. Recurring attacks of erysipelas may result in a permanent lymphedema—the so-called “elephantiasis nostras.”

Treatment

Treatment of erysipelas cases includes *bed rest*, *sponging* for high temperature, *cold compresses* of magnesium sulfate and an *ice bag*. For many years prior to the introduction of more modern methods of treatment the ice bag was the main reliance in cases admitted to the contagious wards of the Cook County Hospital. In addition an ointment of *sulfonated bitumen and glycerin*, equal parts, was applied to the advancing border. *Collodion* painted ahead of the lesions was at one time advised but will rarely stop the spread.

In the last fifteen years the introduction of the *antitoxin treatment* by Birkhaug has marked an important advance, the period of disability being reduced by at least 50 per cent. Symmers and Lewis favor the intramuscular use of the antitoxin and of ninety-two patients with facial erysipelas treated at Bellevue Hospital 85 per cent were cured in three to seven days. The mortality in the facial type was 6.5 per cent and in cases involving the trunk and extremities it was 10 per cent. Symmers emphasizes the fact that the antitoxin treatment does not confer immunity, since recurring attacks occur with the same readiness as when the condition is treated by other methods. Birkhaug, however, has been able to immunize patients against recurring attacks of erysipelas

with the *toxic filtrate of Streptococcus erysipelatis* by giving biweekly intramuscular injections of 500, 5000 and 50,000 skin test doses of the extracellular and intracellular toxins obtained from broth cultures. Tauber also found that erysipelas antistreptococcus serum in 10 to 20 cc. concentrated dose, when given early, produced a prompt amelioration of the toxic symptoms of the disease and gave astonishing results. In recent years *convalescent serum* has also been found of value.

Another important advance in the treatment of erysipelas is by intensive *ultraviolet light irradiation*, credit for which must be given to Ude of Minneapolis, although prior to this Platou and Rigler (1926) reported favorable results from unfiltered roentgen irradiation. According to Ude and Platou's comparative study a single treatment with ultraviolet light, using an exposure time of twice the erythema dose, produced a clinical arrest with the first treatment in 92 per cent of the cases. Titus has recently modified the technic of irradiation, giving from five to twenty times the erythema dose and exposing a margin of 2 inches or more beyond the edge of the lesion.

In the last few years (1936) the spectacular results of *sulfanilamide therapy*, its economy and ease of administration have definitely swung the balance in favor of chemotherapy. The mortality has been still further lowered by sulfanilamide therapy (2 to 3 per cent) and our experience in a small group of cases confirms the position of this drug as the outstanding method of therapy. However, in severely toxic cases and in those showing evidence of intolerance to the drug, reliance should still be placed on the antitoxin.

FURUNCLE

A furuncle is a localized staphylococcic infection having its origin in a hair follicle or its associated sebaceous gland. The ordinary boil usually becomes perifollicular, undergoes liquefaction and central pustulation, and often will open spontaneously, discharging its core, after which healing takes place with a slight scar formation.

Favorite locations are the nape of the neck, the buttocks,

axillae or other sites where there is friction. Boils may occur regionally, recur in crops, or be disseminated in hairy parts. In patients with lowered resistance they may recur over a long period and in diabetic and elderly patients they may prove serious. Staphylococcic septicemia not infrequently has its origin in a boil, especially when it is located around the nose, the upper lip, the perineum or anal region. Incision and improper surgical treatment of "unripe" boils will permit infection to spread to surrounding tissue and favors dissemination into the blood stream.

The *diagnosis* of boils presents no difficulty, although we have seen a number of instances in which a boil was mistaken for a gumma. Furunculoid lesions also occur in various drug eruptions such as bromodermas, in deep-seated fungus infections and in certain tropical skin diseases (Allep-po boil).

Treatment

The treatment of boils varies with the stage of the lesions, their location and extent of dissemination, and is dependent to a certain degree upon the associated systemic factors and the constitutional background (e.g., diabetes, cachexia).

Single boils may be treated by the intermittent application of *hot boric wet dressings* until softening occurs. A simple *incision* of the fluctuant mass may be all that is required. Unnecessary squeezing or manipulation should be avoided. *Adhesive plasters* in the vicinity of the boil should not be employed nor is too early incision advisable.

Many years ago Dr. George Henry Fox suggested a simple, safe and effective method of treating individual boils. As soon as the boil has pointed, a sharp-pointed wooden applicator dipped in 95 per cent *phenol* is bored into the softened tip of the boil. The surrounding skin is then washed in peroxide of hydrogen or a 1:1000 bichloride of mercury solution and an ointment of 5 to 10 per cent *salicylic acid* is applied on gauze and laid over the boil. Another of the older dermatologists, Dr. George T. Jackson, found that boils may be aborted by injecting a drop or two of 5 to 10 per cent solution of *carbolic acid* into the base or touching the top

with pure phenol followed by the salicylic acid ointment. Meticulous care in the dressing of boils will prevent the development of satellite furuncles. Some authors feel that wet dressings, particularly those made with strongly irritant solutions (e.g., bichloride of mercury), are contraindicated after a boil has been incised. Others prefer incision with a fine point of the electrocautery.

For the local dressing of boils we have found one of the three following agents useful: (1) *staphylojell* (Lilly) or *streptojell* as a local immunizing agent; (2) equal parts of *sulfonated bitumen* and *glycerin*; (3) a paste of 5 to 10 per cent *salicylic acid*. *Scarlet red ointment* is useful in the after-treatment.

In addition to these measures the modern *roentgen therapy* for furuncles is an extremely useful adjuvant. A dose of 75 to 150 roentgens ($\frac{1}{4}$ to $\frac{1}{2}$ skin unit), repeated in twenty-four to forty-eight hours, may cause a rapid absorption of the follicular infection. In disseminate furunculosis *sunshine* or *ultraviolet irradiation* may also be recommended.

The relationship between *diet* and susceptibility to skin infections has been stressed by Kulchar, Greenwood, Pillsbury and others. In protracted cases of furunculosis, even in the absence of diabetes or a high blood sugar count, the carbohydrate and sugar content of the diet should be reduced and alcoholic drinks forbidden. Paradoxically, Tauber in 1933 found that the blood sugar in furunculosis was lower than in other skin diseases and that a high carbohydrate diet plus liver extract and the intravenous injections of 500 cc. of 5 per cent glucose was strikingly successful. These observations have not been confirmed.

The value of drug therapy in furunculosis is open to question. *Baker's yeast*, much advertised in the daily press, is of doubtful value. Fresh *brewer's yeast* or brewer's yeast tablets are definitely more efficacious. Following the suggestion of Wright we have found that the combination of tin proteinate, 1 grain, and dried brewer's yeast, 4 grains, is of value in pustular acne as well as in staphylodermas. *Liver extract* is of definite value in pyogenic infections (Sutton). The value of *manganese compounds* given by intramuscular in-

jection is questionable. Oliver and Crawford advise colloidal manganese in pyogenic staphylococcus infections. Sullivan on the other hand could find no sound experimental or clinical basis for its use. In our own work we have been impressed with the occasional value of manganese butyrate in severe staphylococcal infections. One or two intramuscular injections, even though they cause a good deal of local reaction, will hasten the softening of a boil and facilitate rapid healing.

In the last few years an extensive literature has appeared on *sulfathiazole* in staphylococcal infections (Boggs, Knoll, Beling and Abell and others). The Committee on Chemotherapeutic Agents of the National Research Council (1941) recommends for cases of large boils and carbuncles an initial dose of 4 gm. of sulfathiazole, and 1 gm. every four hours thereafter for seven days—in addition to hot fomentations and incision when fluctuation has taken place. Our own experience in a few cases has been highly favorable.

Immunization

Immunization in prolonged sieges of furuncles may be attempted with a variety of methods. *Autogenous vaccines* are preferred by some while others find *stock vaccines* equally valuable. The value of *Bestedka's antivirius* both in theory and practice has not been universally accepted. The same applies to the staphylococcus *bacteriophage*. Recently, favorable reports have appeared on a staphylococcus *toxoid* (Dolman) which is said to give an increase in the antihemolytic titer of the serum. Nonspecific methods of immunization with *foreign proteins* (aolan, activin) are still being used. Staphylococcus *antitoxin* in large doses has been found useful in staphylococcal septicemia (Goldberg and Bloomenthal).

If furuncles continue to develop in spite of immunization, every effort should be made to keep the patient's skin as sterile as possible, and by careful hygiene to prevent reinfection. This includes stress on frequent bathing, the free use of soap, daily change of underwear and bedding, the use of mild antiseptic solutions locally, sunlight and a low carbohydrate diet. Axillary hydradenitis is best treated with x-rays.

CARBUNCLE

A carbuncle is similar to a large furuncle except that it has multiple areas of fluctuation and a broader and deeper area of induration (Fig. 20), is more painful, and is less respon-



Fig. 20.—Carbuncle.

sive to local applications. In general it is far more dangerous on account of the severity of the associated constitutional symptoms, particularly in diabetics, chronic alcoholics and enfeebled elderly individuals.

Treatment

The treatment of carbuncles today is largely a radical surgical procedure, although conservative measures may be tried for a limited period of time. In our own experience in a small number of cases we have been able to obtain a cure by a combination of *roentgen therapy* similar to that used in furuncles, with *hot fomentations*, *local antiseptics* and *manganese butyrate* by intramuscular injection. Under this treatment in favorable cases the infiltrated areas soften, discharge

freely, and after sloughing is finished healing slowly takes place. *Sulfathiazole* may also be used in carbuncles although they respond less quickly than do furuncles. Melton found that many carbuncles will cease to extend after the administration of the drug has begun.

A valuable method of treating carbuncles with *short wave diathermy* has been described recently by Milton G. Schmidt. Employing the inductotherm, treatments were given with a 12 inch disk, low intensity, twenty minutes every hour, twenty-four hours per day for fourteen days, and less frequently thereafter. Severe pain was rapidly alleviated after the first few days and general symptoms subsided rapidly. Complete sloughing occurred by the thirteenth day and subsequent epithelization was accomplished with narrow strips of adhesive tape. Total hospitalization averaged nineteen days. The method employed by Schmidt is obviously one that requires a meticulous and exacting technic but it has certain advantages over the radical surgical treatment that is usually advised. Even in diabetics, successful results were obtained and scarring was decidedly less than with surgery.

The usual method employed by surgeons nowadays is a radical *excision* of the whole mass with the scalpel or the electric cutting current. Surgical treatment appears to be still the optimal method when heat and x-rays fail to delay the progress of the infection or when the special technic of short wave diathermy used by Schmidt is not available.

THE TREATMENT OF ECZEMA-DERMATITIS IN ADULTS*

HERBERT RATTNER, M.D.†

THE development of eczema is dependent upon so many factors and its clinical picture is so variable that its treatment is necessarily one of rational therapeutic measures used intelligently. Eczema of wide extent requires treatment different from that given to a small patch. Acute eczema with vesicles and swelling is certain to be aggravated by treatment ordinarily given to a lichenified patch, and, similarly, eczema due to contact with a cosmetic presents less of a therapeutic problem than does a similar type of eczema caused by pollens.

The modern concept of eczema is that it is a symptom complex with many etiologic factors, particularly those of a sort to make up a predisposing background. Stokes has coined an expressive phrase for it: "Multiple factorial etiologic concept," and he mentioned such causative factors as the hereditary, ichthyotic, seborrhoeic, pyogenic, bacterial, psychic, neurogenic, allergic, metabolic and the factor of focal infection. One or more such factors can usually be demonstrated in a person with eczema—a person whose skin, because of hypersensitivity, either acquired or congenital, responds abnormally to a substance that is ordinarily innocuous. Such factors, if amenable to therapy, should be eradicated; others may be disregarded. Their importance is everywhere acknowledged, yet despite the unusual attention given to them in recent years, the successful management of a case of

* There is much in medicine that is debatable ground. The question as to whether or not eczema and simple dermatitis are the same disease is still being discussed and, because this clinic is given to a consideration of treatment, and in the interest of simplicity, the terms "eczema" and "dermatitis" will be used interchangeably.

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eczema is still today dependent to a greater extent upon proper topical treatment.

There is no specific remedy for eczema in the ordinary sense of the term; one must employ instead well established principles of treatment. These principles and their application can perhaps best be illustrated by reports of a few typical cases encountered in hospital and office practice. The first case is one of acute dermatitis, the kind of case that is most frequently encountered.

DERMATITIS FROM HAIR DYE

CASE I.—A woman, aged fifty-three, entered the hospital because of an intense dermatitis with swelling of the face, eyelids and ears. The oozing skin was red, scaly and crusted in areas, and on the temples the patches were vesicular. The onset followed an application of a certain hair dye which had been used with impunity for several years, but this time a new bottle of the dye had been used. The patient had tried self-medication for a week before entering the hospital, with the unhappy result that there was considerable itching dermatitis venenata from ointments superimposed upon the original eruption; and she was near exhaustion from lack of sleep.

Relief of Itching

For immediate relief the patient was given an injection of *strontium bromide*, 1 ampule of which contains 15 grains of bromide in 10 cc. of fluid. This afforded several hours of comfort from itching and burning and made a break in the vicious cycle of itching and scratching. When necessary, this injection can be repeated before the patient retires and again once each day for a few days; or a mixture of calcium and a bromide would serve as well.

Cold Wet Packs

Cool, soothing, wet packs of *aluminum subacetate* solution were then applied to the patient's head, face, ears and neck. A smooth mask made of several layers of bleached cheesecloth (or bedding, shirting, or any meshed linen material) soaked with the solution was then applied on her head and this in turn was covered with a thin sheet of wax paper,

and over all a bandage. (A pliable cellophane can be used instead of wax paper.) This type of dressing is soothing for only a few hours. When the patient notices that the dressing causes a burning sensation, it must be changed, for the addition of new solution through an opening in the dressing is not satisfactory.

This dressing serves several purposes. It removes the crusts, scales, and débris; and, by its macerating effect, opens the vesicles, maintains a continuous drainage, and exerts a keratolytic effect. Then, too, by maintaining a constant temperature, it exerts a soothing effect, the first step necessary for recovery.

In this case a solution of aluminum subacetate was used because it is a drug of established value in acute inflammations of the skin. A concentration of 0.5 per cent solution can be applied safely to any part of the body. Occasionally, however, aluminum subacetate solution proves to be irritating to the skin of the patient. When this occurs, any one of a number of substances may be substituted for it. A saturated solution of *boric acid* usually serves well, or a dressing with *skimmed milk* is particularly soothing. One may incorporate 0.5 per cent solution of aluminum subacetate solution in the milk and make an excellent preparation. *Normal saline solution* in a dressing is also effective, but it does have a tendency to produce a drying effect upon the skin. *Lime water*, or lime water combined with milk, may be employed; or *lead subacetate solution*, 1 part diluted with 15 parts of water. It is better, however, not to use lead on skin that is eroded or abraded. In general those preparations that are slightly acid exert a more beneficial effect upon eczematous skin, which is alkaline in reaction.

In the presence of secondary infection a solution of *potassium permanganate*, 1:3000, is most effective though it may leave a stain which, however, soon wears off. A dilute solution of 0.25 or 0.5 per cent *silver nitrate* is also effective for weeping and imperigenized eruptions. Obviously, then, the number of agents that can be used for acute eczema is large. Their actions are either similar or they are overlapping and, instead of using them all, one finds by experience and intel-

ligent application that familiarity with but a few gives more assurance and in the end better results.

Wet dressings used for eczema are best used *cold* for their anesthetic effect. Of course, cold dressings should not be applied to too great a body area at one time, for they are apt to produce a chill. Perhaps, too, they should not be applied to the chest or neck of an older person. It is our practice here at the hospital never to apply cold wet dressings to more than one third of the body surface, and never to apply them to an area of the skin with poor circulation. It is important that the dressings be kept moist so as not to irritate the skin, and in ambulatory cases cold wet dressings are not used overnight if the home is not heated.

Ointments

The application of a wet dressing is a laborious task and requires patience. It is not to be employed any longer than is necessary. In this patient with the hair-dye dermatitis, for example, after a few days of continuous wet packs, a bland ointment was used overnight and then throughout the day. The ointment at first used was:

- (1) R Aquaphor,
Aqua dist. aa

This preparation is a soft water-in-oil mixture that spreads easily and is tolerated by all but the exceptional skin. It should be used with caution in persons who have a true sensitization to wool, even though aquaphor is supposedly free of wool fat.

After a few days it was thought best to change to an ointment with more body to it, for greater protection and comfort. The following formula was applied:

- (2) R Unguentum aqua rosae,
Vaseline aa

This is a pleasant mixture that can be readily dispensed anywhere. Occasionally patients prefer a heavier paste such as:

- (3) R Zinc paste, plain 3 parts
Vaseline 1 part

For ambulatory patients, particularly women, an ointment with a color more nearly approximating that of the skin is preferable, such as:

(4) R. Ichthyl	15 per cent
Zinc oxide	10.0 per cent
Calamine	10.0 per cent
Unscented cold cream	qs. ad

Subsequent Care

In this woman's case, the hair was washed frequently, with care given to protection of the skin of the forehead and face, and during sleep the hair was wrapped in a bed cap. She was cautioned, of course, never again to use the hair dye. The use of water and soap for her face was forbidden until the eczema had healed; then, and for several weeks after, she was to use superfatted soap and water that had been softened by the addition of starch.

DERMATITIS, SUPPOSEDLY PSYCHOGENIC, FOUND TO BE OF EXTERNAL ORIGIN

CASE II.—A. S., a boy aged seventeen, was seen with an acute dermatitis of the face similar to that in the previous patient. In addition, the cubital spaces, popliteal areas and dorsal surfaces of the hands were involved. The patient was confined to his home with a nurse in attendance.

The story as related by his mother was essentially as follows: The boy was one of twins, not identical, and since infancy had been less attractive than his brother. His progress at school was slower and from early childhood he had required the help of a child psychologist. He had suffered from infantile eczema and in later years had had several mild attacks of contact dermatitis.

One week prior to this acute attack he had returned from preparatory school with a scholastic report that was far inferior to that of his brother. His father, an uncompromising business man, had taken him severely to task and that evening the boy broke out with eczema—a supposedly psychogenic eczema brought on by an emotional upheaval. There was some improvement in the next few days, sufficient for him to attend a social event four nights later. He attended this affair with his brother; each escorted a girl, and, to add to the patient's discomfiture, the brother's partner was the prettier girl. The consequent frustration

caused a flare-up of his dermatitis and his father, who "couldn't understand such things," again had words with him. Again there was a flare-up of the eczema. The necessary factors for psychogenic eczema were all present, including the readiness of the mother to accept the situation and a misunderstanding father who was largely to blame for the boy's outbreak. Indeed the father was to blame, albeit innocently, for subsequent examination determined that the eczema was due to the father's hair tonic which the boy had used on his return home, and again the night of the party.

This case emphasizes forcefully the dictum that in adults the more one seeks an external cause for simple inflammatory eruptions, the more cases will he identify.

The *treatment* instituted was the same as that used for the previous patient, with strontium bromide intravenously for three days, cold wet dressings of aluminum subacetate and bland ointments. The case is cited, however, as an excellent example of the "multiple factorial etiologic concept."

ATOPIC ECZEMA

CASE III.—Mr. H., aged thirty-two, had had eczema during infancy, and several times during childhood he had suffered from mild attacks of dermatitis with spontaneous remissions and recurrences in the fall and winter. The present attack, the most severe he had yet experienced, began early in June. It consisted of an erythematous papular eruption which involved the eyelids, neck, ears, chest, axillae, cubitals, popliteals and groins. The family history suggested the diagnosis of atopic dermatitis, an eruption which responds to treatment most unsatisfactorily. He had been in the hands of an allergist who found by skin tests that his skin reacted abnormally to a number of agents, but the information was of no practical help.

The areas with acute dermatitis were treated with wet dressings, the less acute areas with bland ointments, the hairy parts with calamine lotion, and the lichenified patches with x-rays. The condition, despite treatment, became progressively worse and it was necessary to take him from his home environment into an air-conditioned room at a hotel. There was immediate improvement, sufficient enough for him to return home after a few days, and the eczema was not particularly bothersome through the next

month. In August, however, with the onset of ragweed pollens, there was again an acute flare-up along with the recurrence of a severe attack of hay fever. This was not unexpected because the results of a study with skin tests gave strong positive reactions to the June grasses and ragweeds.

Treatment of Acute Phase

The treatment of this type of case is beset with difficulties. In general, the choice of palliative treatment depends entirely upon the morphologic characteristics of the eruption. The acute stage is best treated, as were the aforementioned cases, with *cold wet packs* and later bland *ointments*. If there is widespread involvement of the trunk and extremities, particularly hairy areas, it may not be feasible to apply ointments. A *powdery suspension* serves best in such cases; such suspensions as the familiar calamine lotion or, as was used in his case, a starch lotion:

- (5) R Liquid paraffin,
Glycerin āā 5 per cent
Zinc oxide,
Starch āā 20 per cent
Aqua dist. q.s. ad

To this may be added *antipruritic drugs* if necessary. Camphor and phenol, each 0.25 per cent, were added to the mixture. Menthol could have been used as well, and a particularly effective antipruritic agent, though it is somewhat more expensive, is liquor carbonis detergens up to 10 per cent.

Treatment of Chronic Phase

There was improvement of the acute phase of the eruption in this patient and the clinical picture then took on somewhat the characteristics of a seborrheic eczema. Because of this, cultures of the stool were made, but, unfortunately, no predominating pathogenic organism was recovered. Had there been one, a vaccine from such an organism might have produced a beneficial result, as it occasionally does in seborrheic eczema. Empirically a mixture of 40 per cent *precipitated sulfur* in vaseline was then applied to the eczema. This mixture makes a paste, whereas one with a low content of

sulfur constitutes an ointment. Such an ointment is apt to prove irritating; the paste did not and its use led to considerable improvement until finally, as with all such measures, there was an apparent standstill.

At this stage it was decided to use a *tar* preparation, for tar has long since proved its worth in chronic eczema. Patients seem to dislike ointments containing tar, so a *varnish* made up of 5 per cent *crude coal tar in chloroform* was painted on all of the patches. This is very effective but has one drawback: it makes the skin look dirty. With ambulatory patients one usually confines its use to covered parts of the body. The preparation has among its features the fact that it does not soil linen and clothes and with it on the skin the patient can bathe. Certain skins will be irritated by it, but, when the skin is not irritated, this is a most valuable preparation for chronic eczema.

In recent years many variants of the ordinary *crude coal tar* ointments have been introduced, some in which the color has been improved upon, others the consistency, and others again claim one type of advantage or another. They have all proved to be effective in certain cases and can be recommended generally, but one learns to have favorites because of familiarity and success with them.

"Nonspecific" Measures

In this case, even with the use of the coal tar, there was improvement only up to a point, beyond which there seemed to be no more benefit. The so-called "nonspecific" measures then had to be employed. Among those most frequently used are calcium, sodium thiosulfate, calcium thiosulfate, fever therapy and autohemotherapy. *Sodium thiosulfate* was given because it is the experience of most dermatologists that it is the most valuable of these. It can be given 1 gm. daily intravenously, but here at the hospital we think that, since we started giving massive doses in the amount of 7 gm. a day by the intravenous drip method, the results from its use have been better. Finally, the old reliable *liquor potassium arsenitis* was administered, 3 drops t.i.d., and, with the use of sodium thiosulfate daily, Fowler's solution and coal tar paint, there

was finally complete recovery. In prescribing liquor potassii arsenitis one should take the precaution to write a non-refillable prescription because of the tendency for Fowler's solution to produce keratoses in susceptible individuals; and such keratoses occasionally degenerate into carcinoma.

VARICOSE ECZEMA WITH ECZEMATIDS

CASE IV.—This patient was a woman of sixty-five years with varicose eczema of several years' duration. After a recent injury, the eczema became acute and there developed a toxic response generally distributed on the body in the form of an eczematid. Her entire skin, because of age, was dry. The circulation of the affected leg was not impaired too greatly.

The varicose eczema was treated as an acute dermatitis with soothing wet packs; and on the trunk there was applied an oily suspension of *calamine liniment*, N.F. With complete rest in bed and the application of this suspension twice a day there was gradual and progressive improvement. Later, when the eczematid had subsided, the skin was greased with the ointment in prescription No. 1.

ECZEMA NUCHAE

CASE V.—This woman, aged forty, reported with a patch of lichenified eczema on the back of her neck just below the hair line. This type of eczema nuchae is peculiar in that it affects only women; and it is seen most often in women with a certain degree of emotional instability. We made it a point to rule out the possibility that this was an irritant dermatitis. This was done by clinical observation and a patch-test study with all the preparations used in her scalp and hair, including hairpins.

Because of the thickening and the location of the patch of eczema, it was thought best to treat it with *roentgen rays*. Fractional doses repeated every week for six treatments effected a good result. In addition, she was given a stimulating mixture of tar with ammoniated mercury:

- (6) R Pix liquid,
 Ammoniated mercury ȳā 2 per cent
 Ung. aqua rosae q.s. ad

ECZEMA ANI

CASE VI.—This man had a subacute eczema ani. He was referred by a grateful patient who had been treated for pruritus ani with x-rays and a tar ointment. In this man's case, however, the eczema was found to be due to sensitization to resorcin contained in a suppository.

The treatment was that of an acute dermatitis, and with *wet dressings* and *bland ointment*, and without the use of x-rays, a cure was effected. The patient was given *aluminum subacetate* solution to apply as wet packs after defecation and for short periods several times during the day. Prescription No. 1 was used the remainder of the time.

CASE VII.—A short, heavy-set man of fifty-two years reported because of pruritus ani. Examination revealed a rather sharply defined patch of eczema, macerated in the center, with overhanging scales at the periphery of the patch. A focus of tinea dermatitis was found in the last interspaces of his toes.

The patient was treated with moist wet packs of *potassium permanganate* 1:3000 solution two or three times a day, and a mild *keratolytic ointment* made up of:

(7) R Salicylic acid	1 per cent
Benzoic acid	2 per cent
Ung. aqua rosae	qs. ad

When he reported to the office, the area was painted with 2 per cent aqueous solution of gentian violet. He had prompt relief from the topical applications, but cure was not effected until the strength of the ointment was doubled some two weeks later.

IMPETIGENIZED ECZEMA

CASE VIII.—A gas station attendant developed dermatitis of the face from contact with motor oil. Consequent to the scratching from the pruritus there developed impetigo.

In a complication such as this, where there arises the question of whether to treat the impetigo or the underlying dermatitis, one must of necessity treat the impetigo. Cold

wet packs of *aluminum subacetate* were applied to the face for a few minutes every day. Then there was applied an *antiseptic ointment* of:

(8) R Powdered sulfathiazole 5 per cent
 Aquaphor q.s. ad

After the impetiginous element had cleared, a bland ointment was applied and there was complete recovery in about ten days.

ECZEMATOID RINGWORM

CASE IX.—Mr. S. R., a man aged thirty-eight, reported with an eruption of the hands and feet. The interspaces between the toes revealed maceration from which mycelia were recovered. The palms and soles were the site of deep-seated vesicles. A diagnosis was made of tinea dermatitis of the feet with dermatophytids of the palms.

Because these cases are usually associated with considerable hyperhidrosis, the patient was given 75 r of unfiltered x-rays to the palms and soles. Then cold wet packs made with *potassium permanganate* solution, 1:3000, were applied to the hands and feet until the skin was macerated. *Whitfield's ointment*, diluted one-eighth strength, was then applied to the palms and soles, and with this regimen there was cure of the eczematous phase. Of course, proper fungicides had to be used on the feet to eradicate the infection there.

COMMENT AND SUMMARY

1. Eliminate all *external irritants* such as soap, water, heat, friction, plants and chemicals. Identify the causative irritant.
2. Treat the underlying *predisposing constitutional factors*, such as foci of infection, faulty metabolism (a dry skin may indicate avitaminosis A or low basal metabolic rate), autointoxication, nervous disturbances, anemia, and so on.
3. The *topical treatment* of eczema is dictated usually by the morphologic changes in the skin. Always begin treatment with soothing bland remedies and gradually increase their strength if necessary. (a) *Acute eczema* is best treated with aqueous dressings, powdery emulsions and pastes. (b) *Subacute eczema* is best treated with a combination of aqueous

dressings alternating with ointments containing tar. Avoid the use of ointments in areas such as the groins or axillae. (c) *Chronic eczema* is best treated with ointments or paints containing reducing agents, roentgen rays, and non-specific stimulation therapy.

4. *Antipruritics* should be prescribed freely, and do not hesitate to use small doses of barbiturates.

Vehicles of Ointments

A recent development in topical therapeutics has been the increased attention given to the vehicles of ointments. Emulsifying bases, oil-in-water preparations, water-in-oil bases, skin-tone preparations, wetting agents, so-called greaseless bases and the like are being introduced almost every day by pharmaceutical houses. As yet, clear-cut indications for their use have not been formulated, although they give promise of being a distinct advance in topical therapeutics. None of them, to my knowledge, has been included in the National Formulary and, until they have been given a more thorough trial by dermatologists, they should not be recommended for general use.

TREATMENT OF PRURITUS

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ITCHING, the most common symptom encountered in dermatologic practice, may be defined as a sensation which produces an urge to scratch. While the exact mechanism of the production of pruritus is not yet fully understood, it is thought that edema or chemical irritation about the endings of nerves which conduct pain is causative.

DIAGNOSIS OF ESSENTIAL OR PRIMARY PRURITUS

Since itching is a common accompaniment of a great number of dermatoses, most of which are inflammatory, a condition in which such secondary itching is manifested should be carefully distinguished from essential, or primary, pruritus, a disorder in which itching is the only symptom and there are no cutaneous changes other than those resulting from scratching or rubbing. Before making a diagnosis of essential pruritus, therefore, it is necessary to make certain that no lesions are or have been present.

Minute attention should be paid to the possibility of an infestation. *Pediculosis vestimentorum*—infestation with the common clothes louse—produces itching predominantly in areas where the clothing is in closest contact with the body, namely, over the shoulders, on the upper part of the back and about the waist. While it may be possible to detect the presence of "insect bites," the predominant lesions in pediculosis are linear excoriations. The presence of pediculi in the seams of the clothing verifies the diagnosis.

A history of generalized pruritus which is increased after the patient has gone to bed is always suggestive of *scabies*. Persons who bathe daily may have so few lesions that the

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diagnosis becomes difficult. Careful inspection of the interdigital folds, the wrists and the genitalia for the presence of burrows is essential to rule out scabies. At times it will be necessary to instruct the patient to forego bathing for a week and then to return for further observation, by which time typical lesions will have developed if scabies is present.

Often a patient who complains of itching has no lesions at the time of the examination but gives a history of urticarial wheals associated with the attacks of pruritus. A tentative diagnosis of *urticaria* should be made in such instances and symptomatic treatment carried out while the cause is sought.

Essential pruritus may be generalized or localized.

GENERALIZED ESSENTIAL PRURITUS

Generalized pruritus is a fairly common complaint. Its causes are so manifold that successful treatment depends on first determining the cause, for purely symptomatic therapy can only allay the symptom temporarily. The causes may be divided into two groups, organic and functional.

Generalized Pruritus of Organic Origin

Among the organic causes "dry skin," or *asteatosis*, is common. The patient with this condition has a slightly dry skin to start with. Then, during the winter months, exposure to an insufficiently humidified and overheated atmosphere indoors, too frequent bathing and the use of too hot water and too much or too strong soap so accentuate the inherent dryness of the skin that itching is produced. Close examination will show that the skin is dry and in some places is slightly chapped. Those parts of the body, however, which are subject to more perspiration, such as the axillae, the genital region and the feet, are always unaffected. Such generalized pruritus—often called "winter itch" or "bath itch"—can be cured easily by such simple measures as increasing the humidity of the indoor air and preserving the oil reserve of the skin by limiting bathing and avoiding the use of strong alkaline soaps. The axillae, genitalia and feet may be washed daily with water and a mild neutral soap, but sponge baths should be substituted for the usual all-over tub bath

with soap and water. In addition, the skin should be oiled (see later).

Among the physiologic states capable of producing pruritus are menstruation, pregnancy and senile atrophy of the skin. Itching associated with *menstruation* is not common and is far less intense than that which often occurs during *pregnancy*. While it is impossible to rule out the presence of an endocrine disturbance during menstruation and pregnancy, a functional basis should not be overlooked, because it is well known that emotional instability is increased during these periods. Therefore, though endocrine therapy is sometimes employed, treatment should usually be that for functional pruritus, which is discussed later.

Senile pruritus, caused by atrophic changes of the skin, is often accompanied by senile cerebral arteriosclerosis. Senile skin, which is dry and thin, should be treated in the same manner as asteatotic skin. Sedatives are indicated.

The skin of patients with an early stage of *acquired hypothyroidism* resembles asteatotic skin, and generalized itching is the usual complaint. A decreased basal metabolic rate will reveal the cause of the pruritus, and adequate therapy will eliminate the symptom.

Diabetes may be associated with severe pruritus. Urinalyses and blood sugar tests are, therefore, indicated in every case of chronic generalized itching. *Hepatic disease* also is a not infrequent cause of generalized pruritus. In this connection it is important to remember that, in cases in which there is an elevated icteric index but no clinical jaundice, intense pruritus may nevertheless be present. Treatment should be directed toward correction of the hepatic disorder.

Other causes of pruritus are *neoplasms* of various types. Carcinomas as well as sarcomas, especially those originating in the abdominal organs, may be responsible. However, most notorious for the production of intolerable generalized pruritus are the lymphoblastomas, or white blood cell dyscrasias. *Leukemia*, *pseudoleukemia*, *lymphosarcoma*, *Hodgkin's disease* and *granuloma fungoides* may be preceded by pruritus of months' or even years' duration before definite changes are evident in the blood or in the lymph nodes. Hence, in

any case of generalized pruritus a complete blood count is indispensable, though the blood picture may be normal at the onset of any of the dyscrasias and it remains normal throughout the course of granuloma fungoides and, at times, of pseudoleukemia. For the demonstration of enlarged lymph nodes, especially in Hodgkin's disease or lymphosarcoma, roentgen examination of the chest is a necessary routine measure. In pruritus due to white blood cell dyscrasias, arsenic in the form of Fowler's solution is helpful. Since the prognosis for life is unfavorable, there is no objection to its use. For other conditions Fowler's solution is not recommended because of the great risk of arsenical complications, including pigmentation and precancerous keratoses, which may follow its prolonged use.

It has been stated by some investigators that chronic *foci of infection* may at times be responsible for generalized pruritus. Though in my experience such occurrences are rare, cases in which chronic cholecystitis, prostatitis and cystitis were causative have been reported, and investigation for the presence of these disorders appears justified.

In cases of *renal disease* in which the blood urea is elevated, generalized pruritus is often present. In both renal and *cardiac disease* the edematous areas are sometimes pruritic. Therapy must be directed toward the underlying disorder.

Pruritus associated with *gout* may be generalized or localized. In the latter case it involves the region of the tophi or the anal area. Measures designed to eliminate uric acid are followed by relief of the itching.

Pruritus may accompany the organic nervous diseases, particularly senile cerebral arteriosclerosis. In such cases the symptom is often aggravated by senile changes in the skin. The cause of the itching is suggested by such factors as the age of the patient, the intensity of the pruritus and the presence of peripheral arteriosclerosis, arcus senilis or sclerosis of the retinal vessels. The symptom is best controlled by intravenous injections of sodium bromide given three times weekly. The initial dose is 20 cc. of a 10 per cent solution, and each subsequent dose is increased by 10 cc. until 30 cc. is reached, after which the injections may be continued as

long as the itching persists and resumed if the itching recurs. Androgen and estrogen therapy may also be of value.

Neurosyphilis of the tabetic or paretic type likewise may be accompanied by pruritus, and at times the suspicion that syphilis was present, aroused by this symptom, has been verified by the results of a general examination. The itching improves with antisyphilitic treatment.

Medicaments may also cause generalized pruritus. Among the drugs which have been found causative are adalin, alcohol, arsenicals, cannabis indica, cinchophen, cocaine, gold salts, nirvanol and opium derivatives. Opium and cocaine addiction and delirium tremens are often accompanied by itching. The obvious treatment is discontinuance of the offending drug.

Generalized Pruritus of Functional Origin

When there are no physical or laboratory findings indicative of an organic basis for the itching, the possibility of a functional basis should be investigated. Functional pruritus is far more common than is generally supposed.

The nervous disorder underlying functional pruritus may range in severity all the way from a simple instability of the nervous system to a true psychosis. While the diagnosis of functional pruritus must be based primarily on a study of the patient's personality and emotional make-up, it is helpful to remember that, in contrast to organic pruritus, which tends to be constant, functional pruritus takes the form of sudden attacks. The attacks, which vary considerably in duration, may come on any time during the day or night but occur most frequently at night when the patient has disrobed and air has struck the skin.

In approaching the problem of functional pruritus, as in any functional disorder, the physician must call on his store of patience, sympathy and tact. Once the suspicion is aroused that the patient's disorder may have a functional basis, every effort should be expended to gain his confidence so that the extent of the nervous disturbance can be determined. Treatment of a full-blown neurosis or psychosis is distinctly the province of the psychiatrist, who alone has had the specific

training and experience necessary to enable him to assume full responsibility for the patient with severe mental disease. Consequently, common sense and discrimination must be exercised in deciding which patients must be referred directly to the psychiatrist and which ones will be suitable subjects for the relatively shallow psychotherapy which the practicing physician can administer along with his treatment of the cutaneous disorder.

There are two common types of *mild emotional disturbances* which can often be alleviated by the understanding and interested physician. The patient with the first variety is best exemplified by the "high pressure" type of business man. Such a patient is obviously under tension, is usually overly ambitious and energetic and is inclined to assume too much responsibility and to take his obligations too seriously. Such a patient needs help in restoring balance to the conduct of his life. The second type of patient, who is more likely to be a woman, often has feelings of insecurity and inferiority. She is inclined to worry unduly and to evaluate incorrectly the essential factors in her life, particularly in the sexual sphere. Such a patient needs help in gaining a perspective toward her needs and interests.

Therapy of such disorders is not difficult, but not all physicians have the attributes which are essential for carrying it out successfully.

Intelligent sympathy and understanding are the two prime requirements without which no physician can hope to carry out successful psychotherapy. A functional disease is a true disease; its symptoms are very real to the patient, and adopting the attitude that he is "not really sick" will vitiate any attempts to get at the underlying emotional problems. A sympathetic understanding implies not a "hand-holding" point of view but a realization that the patient needs assistance in solving his difficulties.

There are two types of physicians who, in spite of interest and sympathy, are unsuited for handling the emotional problems of patients with functional disease. The first is the type of physician whose experience is so limited that he is fre-

quently faced with patients whose personalities, background and life situations he is incapable of understanding. He is likely to blunder in trying to reduce a complex emotional pattern to his own simple formula without taking sufficient cognizance of factors which, though strange to him, are of great importance to the patient's welfare. One must remember that "normal" covers a wide range in sexual, social and moral, as well as physical, spheres.

The second type is the physician who has unsolved problems of his own which are likely to bias his approach and to distort his therapeutic attempts. He will often do positive damage by reinforcing abnormal trends in the patient which parallel the course of his own difficulties or by failing to recognize important factors because they play a role in his own problems.

However, the physician who is equipped with the necessary attributes and a good measure of common sense can greatly aid the patient in unraveling his emotional problems. In addition, there are several practical means by which he can reinforce the effects of therapy. For instance, he can often help to eliminate causes of friction by interviewing marital partners or relatives and by suggesting alterations in living arrangements. He can assist in outlining a regimen which will provide for adequate rest, including daily naps and regular sleeping hours. He can insist on a healthy balance between work and play and point out the value of restful vacations. The relaxing beneficial effects of daily sunbaths have been well established. The acquisition of an ultraviolet lamp to provide artificial sunshine during the winter months is a warranted investment. Sedation is often a necessary adjunct to the foregoing therapeutic suggestions.

Local Therapy

The local therapy, which has only a temporary effect in generalized pruritus, must always be secondary to the correction of the underlying cause of the disorder, but local measures must often be instituted for symptomatic relief. An oily lotion should be used especially if the skin is dry,

as for example in asteatosis or senile pruritus. *Cook's emulsion base*, which is a satisfactory preparation, has the following formula:

R Olive oil	190.0
Oleic acid	20.0
Triethanolamine	4.0
Water	q.s. ad 360.0

Among the satisfactory antipruritic local applications which may be used in all forms of generalized pruritus are *Pusey's calamine liniment*:

R Tragacanth pulv.	4.0
Phenol,	
Glycerin	āā 0.66
Calamine,	
Zinc oxid.	āā 30.0
Ol. oliv.	120.0
Oil of bergamot	2.0
Aq. dest.	q.s. ad 480.0

and *menthol-phenol paste*:

R Menthol	0.15
Phenol	0.6
Ac. boric.	3.0
Zinc oxid.	15.0
Petrolat.	45.0
Ungt. aq. ros.	q.s. ad 120.0

A warning should be given against the prolonged use of lotions, such as the calamine lotions, because of their markedly drying effect, which will aggravate pruritus from any cause.

The use of soap and water must be curtailed. The only bath permissible is the *colloid bath*, which has a mildly antipruritic effect. Directions are as follows:

1. A gruel is made, the amount prepared depending on the size of the tub, by boiling 1 to 2 cupfuls of oatmeal in 1 to 2 quarts of water; water is added continually so that the volume of the mixture is maintained, and the boiling is continued until the gruel is of moderately thick consistency. It is then set aside to cool.

2. The cooled gruel is poured into a large gauze bag, tied securely and the bag swished around in the tubful of water until nothing but husks remain in the bag. The water should become whitish and opalescent.

3. After the colloid bath, which lasts from ten minutes to two hours, the patient dries himself by patting (not rubbing) with a towel.

The use of soap should be restricted to the feet, genitalia, axillae, face and hands, and for this purpose a superfatted soap, such as Basis Soap, Hazeline Soap, or lanoline soap, is recommended.

LOCALIZED ESSENTIAL PRURITUS

Localized pruritus occurs predominantly in three locations: around the anus, on the genitalia—especially in women—and on the scalp.

Pruritus Ani

Pruritus ani, like generalized pruritus, may have either an organic or a functional basis. Among the *organic causes* are intestinal parasites, such as pinworms, which are more common in children than in adults; intestinal neoplasms, such as carcinoma of the colon; gout, and diabetes. The role of hemorrhoids and anal fissures in the causation of pruritus ani has been overemphasized; they play a minor part, if any, in its production. The stools should be examined for ova and parasites to rule out the presence of pinworms, and proctoscopic examination should be performed to eliminate the possibility of neoplasms. Essential pruritus ani must be distinguished from intertriginous fungous infections, especially those due to monilia, which are not infrequent in this area because the warmth and moisture encourage their growth. The presence of erythema and scaling should arouse suspicion; microscopic examination will reveal the fungi.

Pruritus ani of functional origin is far more common than that of organic origin. In an overwhelming majority of the cases of pruritus ani which I observed at the University of Chicago Clinics over a period of twelve years, the disorder was of functional origin. The same considerations which were previously elaborated with regard to the diagnosis and treatment of generalized functional pruritus are valid for the localized variety. That emotional disturbances are causative is established with greater ease in functional pruritus

ani than in any other form of functional cutaneous disease. Patients with functional pruritus ani gave evidence of disturbances in the sexual sphere with almost monotonous regularity.

Local measures are important and must be carried out with minute attention to detail. To avoid irritation the softest type of toilet tissue and a minimal amount of rubbing must be used, and the cleansing of the anal region should be completed with small pledgets of cotton soaked in mineral oil. During the daytime Pusey's calamine liniment should be applied. The sharp edge of a wedge of cotton is soaked with the liniment and inserted between the nates, for the double purpose of applying the mildly drying, antipruritic medicament and of keeping the skin surfaces apart to avoid further maceration. At night menthol-phenol paste is applied, and the surfaces are kept apart by cotton or gauze. In cases of severe and resistant pruritus, roentgen therapy is given to relieve the itching temporarily and to permit the patient to obtain more rest. Roentgen therapy is in no way curative; it must be used cautiously, and its limitations should be appreciated. After pruritus has been present for a long time, the habit of scratching has become so fixed that it must be combated by strict measures. It is sometimes necessary to restrain scratching during sleep by having the patient's hands tied or by having him wear ordinary workman's gloves. The fingernails should be filed down to prevent damage to the skin if he should scratch.

The injection of nerves and other *surgical procedures*, such as nerve section or excision of the pruritic area, are mentioned only to be condemned.

Pruritus Vulvae

Pruritus vulvae may likewise have an organic or a functional basis. An infection of the cervix or vaginitis caused by trichomonas may be associated with a discharge which is sufficient to cause pruritus but not profuse enough to be clinically evident. Any pelvic abnormality should be corrected. As in pruritus ani, care should be taken to rule out the presence of fungous infections. In the majority of cases

chronic recurrent pruritus vulvae has a functional basis, and evaluation and treatment of this disorder should be undertaken with that fact in mind.

Kraurosis vulvae, a condition of obscure origin associated with intractable itching, is easily confused with functional pruritus; it is always characterized by inflammatory phenomena and ultimate atrophy. Since it has its onset after the menopause, the patient with kraurosis is considerably older than the average patient with pruritus vulvae.

As a *local application* for all forms of pruritus vulvae, calamine liniment or liquor carbonis detergens lotion (see later) may be used.

Pruritus of the Scalp

Pruritus of the scalp, which is of functional origin and fairly common, must not be confused with secondary pruritus produced by seborrhea (dandruff) and by seborrheic dermatitis; it must also be distinguished from secondary pruritus caused by infestation with *Pediculus humanus*. The patient often complains not only of itching but of cutaneous lesions, which he erroneously thinks are responsible for the pruritus. Inspection will reveal only small excoriations with sanguineous crusts. General therapy should be directed toward correction of the emotional imbalance which is responsible.

Local treatment consists of frequent shampooing with tincture of green soap. A thin film of 5 per cent ammoniated mercury ointment, rubbed into the scratched areas of the scalp in the evening, will prevent and control secondary pyogenic infection of the excoriations.

Neurotic Excoriations and Acarophobia

These are functional disorders which can only be briefly mentioned here. Neurotic excoriations, which vary in size and depth, result from the patient's irresistible urge to scratch and dig the skin.

Attempts to educate the patient and help him gain insight into the nature of the emotional problems responsible for his

disorder are not often successful. In most cases the condition is a true neurosis, and the patient should be referred to a psychiatrist.

SECONDARY PRURITUS

The local therapy of secondary pruritus consists in treating the dermatosis, of which the itching is one symptom. Since the management of the many dermatoses which give rise to secondary pruritus differs greatly, only general suggestions which are applicable to all of them will be given here.

Avoidance of Overtreatment

There is a widespread tendency to overtreat dermatoses and to employ strong applications when mild ones are indicated, often with disastrous results. The use of too strong ointments always causes a temporary aggravation of a dermatosis. It must not be forgotten that in addition, in certain predisposed patients, such overtreatment of psoriasis, lichen planus or any dermatitis, including eczema, may result in the development of generalized erythroderma and exfoliative dermatitis. Upward of a year is often required to correct the damage from such ill advised therapy. Therefore, it cannot be emphasized too repeatedly that mild applications should be used until the physician has become well acquainted with the reactivity of the patient's skin. Cognizance should be taken of the patient's comments, and any application which he finds irritating should be discontinued immediately. There is still an unfortunate tendency among the lay public to consider as efficacious an ointment which makes the eruption ooze, because it "drives out the poison from the skin." Obviously, any topical application which stimulates exudation cannot have any but an irritating effect.

Wet Dressings

A weeping surface is always best treated by means of wet dressings; the most rapid drying, and at the same time anti-pruritic, effect is achieved by the application of open, or dermatologic, wet dressings. Solutions for wet dressings

should be freshly made every four hours. I use *potassium permanganate*, 0.65 gm. (grain 1), in one pint of water routinely except when the resulting temporary discoloration of the skin is objectionable, in which cases *liquor alumini subacetatis*, 1:16, or *hydrosal*, 1:20, is substituted. Wet dressings are applied as follows:

Several pieces of gauze are kept soaking in the solution, which should be maintained at room temperature. A piece of the soaked gauze is applied to the affected area about every five minutes. The dressing should not be covered and must never be allowed to dry out on the skin.

Wet dressings should not be applied to more than one third of the body at one time and care should be taken to avoid chilling of the patient.

Lotions and Ointments

Since wet dressings are not feasible at night, soothing applications should be used. In general, lotions are better tolerated by an oozing skin than pastes or ointments. Calamine liniment is satisfactory. Colloidal, or starch water, baths should be substituted for the ordinary soap and water cleansing.

After exudation has diminished, plain aquaphor or an ointment containing 3 per cent ichthyol in aquaphor may be applied. Menthol-phenol paste is also satisfactory. If a lotion is preferred, *liquor carbonis detergens* (*liquor picis carbonis*, N.F.) is a good antipruritic. It is used in from 5 to 50 per cent concentration. A satisfactory mixture for use on unbroken skin is the following:

R Liqu carb deterg.	4S 0
Zinc oxide,	
Talcu	āā 50 0
Glycerin	24 0
Alcohol, 50 per cent	qs. ad 240 0

In all pruritic dermatoses *rest* and *sedation* are indicated. The administration of a phenobarbital compound is always helpful except in those drug eruptions in which hypersensitivity to a sedative is suspected.

COMMENT

In the management of pruritus and of pruritic dermatoses the following admonitions should be borne in mind:

First, determine the cause; and if that should prove impossible in the beginning, at least rule out the presence of any internal disorder which might be responsible.

Second, give the patient symptomatic relief by prescribing sedatives and by using local applications which will soothe but under no circumstances irritate.

Third, study any patient who has chronic recurrent pruritus from the functional point of view. A common sense evaluation of complicating or underlying emotional difficulties will often aid in restoring the functional stability of the nervous system. The emotional catharsis which a patient may experience through his relationship to an understanding and sympathetic physician can be an important factor in his recovery from a chronic recurrent pruritus of "obscure origin."

BIBLIOGRAPHY

Becker, S. W. and Obermayer, M. E.: *Modern Dermatology and Syphilology*. J. B. Lippincott Co., Philadelphia, 1940.

X-RAY AND RADIUM TREATMENT OF DISEASES OF THE SKIN

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A SYMPOSIUM on the "Treatment of Diseases of the Skin" would be incomplete if x-ray and radium were omitted. In this article, radiotherapy is referred to as the treatment of disease by the application of x-rays and radium, omitting ultraviolet and other radiations owing to lack of space.

The dermatologist should know why, when and how radiotherapy is used in dermatology. Since there is little, if any, difference between the biologic and therapeutic action of x-rays and radium, they will be discussed together. Because they are similar the indications are alike for each agent. This clinic is a mere outline of the technic and dosage used, the diseases which are amenable to treatment, and the general results to be expected. The reader is referred to MacKee's textbook¹ for a complete presentation of the subject. I have borrowed freely from his work, as it is a standard for English-speaking dermatologists.

Since the discovery of x-rays in 1895, and of radium in 1898, these sources of energy have been utilized in dermatology. At first, x-ray treatment proved of value in lupus vulgaris and carcinoma of the skin. Following these results, overenthusiastic claims were made for x-ray therapy, even in many incurable diseases. Overenthusiasm still prevails in some quarters.

What are the reasons for the use of radiotherapy? They are based on the experimental and practical work which has established that more than eighty diseases of the skin are responsive to treatment with x-rays. In a few diseases a cure can be obtained only with radiotherapy and in a few more

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diseases temporary relief is all that can be derived from this agent. Many dermatoses are treated by combining x-rays with other methods of treatment. The statement was made many years ago by William Allen Pusey that: "It is, in fact, hardly too much to state that roentgen ray therapy is the most useful addition to the treatment of cutaneous diseases that has been made." The modern dermatologist could not practice efficiently without radiotherapy.

EFFECTS OF RAYS ON LIVING TISSUE

The changes that are produced by radiotherapy upon living tissue were summarized in the early part of the present century by William Allen Pusey and with a few exceptions still hold good. They are as follows:

1. Functional inhibition and atrophy of the cutaneous appendages.
2. The environment may be so modified that bacteria and fungi may encounter a less favorable medium upon which to grow.
3. The nutrition of the living cell is affected. Small amounts probably stimulate while larger doses inhibit cell function. Very large amounts produce complete cell destruction. It is probable that all therapeutic effects are produced by the inhibitory or destructive action of the radiation.
4. The inhibitory and destructive action is much more pronounced on immature cells and cells in the active state of divisions than on cells that have acquired their fixed adult morphologic or physiologic characteristic (law of Bergonie and Tribondeau); also on cells that are physiologically active, such, for instance, as the cells of the sweat glands; and on lymphoid tissue.
5. There is an anodyne and antipruritic effect either primary or secondary.

THERAPEUTIC INDICATIONS

From the foregoing it may be adduced that x-rays have possible indications in the following groups of cutaneous affections:

1. Conditions in which it may be desirable to remove hair

either temporarily or permanently: (a) selected cases of hypertrichosis; (b) selected cases of nevus pilosus; (c) sycosis; (d) tinea tonsurans.

2. When it is desired to reduce the activity of the sebaceous glands: (a) comedo; (b) acne vulgaris; (c) acne rosacea; (d) seborrhea oleosa.

3. When it is desirable to lessen the function of the sweat glands: (a) hyperidrosis; (b) bromidrosis; (c) chromidrosis; (d) pompholyx; (e) hydrocystoma.

4. The indirect effect on bacteria and fungi in tissues may play a role in a number of affections, such as tinea, acne and sycosis. In many of the bacterial affections such as acne, and fungous affections such as dermatophytosis (eczema due directly or indirectly to fungi), the result may be due to the inhibitory action of young and active cells on lymphocytes and on chemical changes occurring in tissue that is being irradiated.

5. Some observers believe that it is the stimulating action of the rays that produces the therapeutic result in inflammations like eczema, psoriasis and lichen planus, but it is the consensus that this effect is caused by inhibition of cell division and activity, and possibly by liberation of antibodies from destroyed lymphocytes.

6. The radiosensitiveness of young cells, that is, cells in the stage of division, embryonic and lymphoid tissue, explains theoretically the therapeutic action of x-rays on malignant neoplasms. the granulomas and some of the benign new growths: epitheliomas, sarcoma, young evolving angiomas, tuberculosis, mycosis fungoides, leukemia cutis, and so on.

7. The anodyne effect comes into play in the treatment of painful malignant and inflammatory conditions and in the pruritic dermatoses.

8. No one yet has been able to evaluate the psychologic effect of treatment with x-rays. In some instances the psychic response may be partly or wholly responsible for the therapeutic results. At times the recovery may be spontaneous and coincidental with such treatment. However, the consensus is that in most instances the therapeutic result is due to the direct biologic effect of the radiation as outlined.

It is evident from the aforementioned summary of the therapeutic indications for x-rays that their field of application in dermatology is extensive. Generally speaking, radiotherapy is indicated in itching, lichenification, infiltrations, thickenings, indurations; new growths and diseases requiring depilation or inhibition of glandular activity. What has been said for x-rays applies to radium.

X-RAY THERAPY IN CUTANEOUS DISEASES

Should the radiologist or the dermatologist apply x-ray therapy, if indicated, in cutaneous diseases? Cutaneous x-ray therapy is a part of dermatology, since it was developed and is being continued by dermatologists. Many physicians and radiologists still believe that x-rays should be tried in all diseases of the skin. A trained dermatologist does not follow this routine. There is no valid reason for it, since forty years of experience with x-ray therapy have shown us which of the dermatoses are more or less amenable to treatment with this agent.

Apparatus

Before the dermatologist buys x-ray apparatus he must choose between *thermionic* (kenetron) and *mechanical* rectification. The principle of the thermionic valve tube is unidirectional transfer of current by the passage of electrons. A mechanical rectifier is a device which, by changing contacts at the proper moment in a cycle, changes alternating into pulsating direct current. It must be admitted that the kenetron valve is gaining in favor and is likely to be used exclusively in the future. No matter what your choice, buy from a reputable manufacturer who can furnish prompt service. Either type is suitable for cutaneous therapy. Assuming that modern equipment is used, the technic applies to either type of rectification.

Measurement of X-rays

Our next and greatest concern is the measurement of x-rays delivered at the site of the disease, either upon or below the surface of the skin. This depends upon the *concentration* of the radiation and the *intensity*.

CONCENTRATION OF THE RADIATION.—Concentration of the radiation is regulated by the penetrability and this in turn by the quality. The quality of the radiation is usually measured by the absorption in aluminum or copper. The thickness of copper or aluminum which absorbs one half of the radiation is called the "half-layer value." Quality is also expressed in effective wave lengths. Quality of radiation is usually indicated by the voltage, but in the near future it may be recorded in half-layers of aluminum or in effective wave lengths.

INTENSITY.—Quantity of x-rays is measured by the standard international unit, the *roentgen* (r), or, in biological terms, *erythema dose*.

Ionization Measurement.—At the present time the most accurate method of measuring the radiation intensity is by ionization. Ionization dosimeters of the thimble type calibrated in roentgens are available, and they provide a quick means for direct measurement of quantity. A physicist should check the quantity and the quality of x-rays at least twice a year.

"The roentgen is the quantity of radiation which, when all the secondary electrons are utilized and the wall effect of the chamber is avoided, produces in air, under standard conditions, such a degree of conductivity that one electrostatic unit of charge is measured at saturation current."

The roentgen is a more satisfactory method of expressing dosage than is erythema dose.

Biological Standards of Measurements.—The basis of the biologic method is the *erythema dose*. It is the quantity of x-rays which will produce a slight redness of the skin within seven days, that persists for one week, then disappears. A trial set-up for an erythema dose would appear as follows: 100 kilovolts at 2 milliamperes for 3 minutes, with an 8 inch distance between anode and skin. If these constants do or do not produce an erythema on sensitive areas of the skin, such as the flexor surface of the forearm and inner side of the thigh, the time factor is varied accordingly.

MacKee has established the following rules or laws that should be memorized:

- "1. The intensity of radiation varies as the square of the voltage.
- "2. The intensity of radiation varies as the milliamperage.
- "3. The intensity of radiation varies as the time.
- "4. The intensity of radiation varies inversely as the square of the distance."

Dosages

The number of roentgens required for the erythema dose has not yet been determined. For all practical purposes, in superficial therapy without filtration and with mechanical rectification, 350 roentgens are considered to be about the equivalent of an erythema dose. If kenetron rectification is used, about 300 roentgens are equivalent to an erythema dose. The slight difference is due to ray quality being softer with kenetron rectification than when produced by mechanical rectification.

It is likely that about *350 roentgens at 100 kilovolts* (chamber in air) will become the standard for the unfiltered erythema dose (mechanical rectification).

I see no harm in selecting these figures as the proper ones, at least for the time being, as they are within the bounds of safety. Radiotherapists expressing intensity in roentgens will be more nearly in uniform agreement than if erythema dose is used. A roentgen is the same in New York as in Los Angeles. This cannot be said for an erythema dose as there are too many factors that control it.

Unfiltered radiation is used routinely for superficial dermatoses. *Filtered* radiation is used for deep-seated lesions and lesions of considerable volume. One hundred kilovolts, unfiltered, with an anode-skin distance of 8 inches is recommended. Most of the extensive lesions can be radiated with this set-up and it is advisable because the hazard of deep penetration is avoided. Anode-skin distances of 12 inches or 16 inches can be used.

Dosage Schedules

Most of the cutaneous diseases are treated with one of the dosage schedules:

Fractional Treatment: 88 roentgens with mechanical rectification; 74 roentgens with kenetron rectification; $\frac{3}{4}$ erythema dose, unfiltered, is the routine dosage for most superficial dermatoses. This amount can be given once a week, but the total should never exceed 1600 roentgens and should usually be less.

Subintensive Dose: 176 roentgens with mechanical rectification; 150 roentgens with kenetron rectification; $\frac{1}{2}$ erythema dose. Not to be repeated in less than three or four weeks.

Intensive Dose: 350 roentgens with mechanical rectification; 300 roentgens with kenetron rectification; erythema dose. Not to be repeated until the end of four weeks.

Hyperintensive Dose: 300 to 2400 roentgens. A rest of five weeks is allowed after complete disappearance of the reaction before the treatment is repeated, depending upon the disease and the dose.

Roentgenization versus Radiumization

Whether to employ roentgen rays or radium in the treatment of a cutaneous disease is a problem that confronts the less experienced dermatologist. In a general way it can be stated that there is little difference between the biologic and therapeutic action of x-rays and gamma rays of radium. They are equally efficacious provided the disease lends itself to treatment with radiotherapy. In practice radium is preferable to x-rays when it is desirable to have precise localization, especially in the mouth, nose and external auditory canal. In these inaccessible regions radium needles and radon are more convenient. Generalized cutaneous diseases are treated more conveniently and rapidly with x-rays. Time is the deciding factor as to the choice of x-rays in the place of radium.

Another item is the question of expense. However, in many cases, especially when the radium is owned by the dermatologist, the expense should be the same for both. This hardly applies when radium is rented from companies that make radium rental a business. Radium companies and institutes that try to impress physicians with the better results obtained with radium are unfair. Another objectionable

practice of many radium companies is the renting of radium to physicians who are unfamiliar with it but who treat an unrecognized disease according to directions furnished by mail. Would these same medical men choose an untrained or inexperienced physician to remove their gallbladders according to written instructions furnished by a surgeon?

MacKee believes that there is some difference between the results obtained with *beta rays* of radium and those obtained with x-rays and gamma rays of radium. For instance, the elevated type of *nevus vasculosus* (strawberry mark) often disappears rapidly following applications of beta rays of radium.

Many authorities are in favor of employing beta rays for leukoplakia as they are perhaps more efficacious. Probably many patients with leukoplakia will do just as well if radium is not used, provided there is no evidence of malignant changes. Of course, patients with leukoplakia should be kept under observation. Some of the keratoses respond favorably to beta rays. Gamma rays are more penetrating; that is, less readily absorbed than x-rays of ordinary wave length. Therefore, they possess an advantage in the treatment of deep-seated lesions. Finally the effect of radium and x-rays is about the same in all other dermatoses.

Technics Employed in the Commoner Diseases

The following commoner diseases are arranged according to etiologic classification as much as possible:

Diseases Caused by Pyogenic Organisms or a Secondary Factor.—1. *Acne varioliformis*: x-rays, fractional method, if local treatment fails.

2. *Acne vulgaris*: x-rays, fractional method; dermatologic treatment important.

3. Carbuncle: x-rays, intensive, 350 roentgens, plus filter.

4. Furuncle: x-rays, 88 roentgens, once or twice a week for two weeks if required.

5. *Granuloma pyogenicum*: remove with actual cautery and treat base with beta rays of radium, full strength, plus $\frac{1}{10}$ mm. of Al for thirty minutes' contact.

6. *Paronychia*: x-rays, fractional method.

7. Rhinophyma: x-rays, fractional method will cause acne-form lesions to disappear and lessen sebaceous activity.

8. Rosacea: x-rays, fractional for secondary acne lesions.

9. Sycosis vulgaris: x-rays, fractional.

Fungous Diseases.—1. Actinomycosis: x-rays or radium filtration.

2. Blastomycosis: x-rays, 264 roentgens once every three weeks for three or four times.

3. Moniliasis: x-rays, fractional to chronic paronychia only.

4. Tinea barbae: x-rays, depending upon organism; 88 roentgens every two to three days, four to eight exposures.

5. Tinea capitis: determine organism by culture. X-rays, epilating dose, with Kienböck-Adamson method of dividing scalp. Permanent cure usually with x-rays.

6. Farus: x-rays to scalp; epilating dose must be a little larger than in tinea capitis. Permanent cure often with x-rays.

Eczema and Dermatitis Group of Diseases.—1. Dermatitis venenata: x-rays, 88 roentgens once a week for a total of four exposures.

2. Dermatophytosis: x-rays, 88 roentgens same as for dermatitis venenata.

3. Dermatophytid: x-rays as in dermatophytosis.

4. Infectious eczematoid dermatitis: x-rays, fractional.

5. Lichen chronicus circumscriptus: x-rays, fractional.

6. Seborrheic dermatitis: x-rays, fractional.

Psoriasis and Lichen Planus.—1. Psoriasis: x-rays, fractional, for face and hands if other methods fail.

2. Lichen planus: x-rays, fractional to control subjective symptoms.

Pruritus.—1. Regional pruritus (anal, scrotal, vulvar): x-rays, fractional method is useful.

Diseases of the Hematopoietic System.—X-rays are of temporary value.

1. Mycosis fungoides: x-rays, fractional to lesions.

2. Leukemia cutis: x-rays, fractional, 88 roentgens to entire cutaneous surface each week for three months if needed.

3. Hodgkin's disease (cutaneous manifestations): x-rays, subintensive with filtration.

Tuberculosis of the Skin.—1. Lupus vulgaris: x-rays, sub-intensive with filtration.

2. Tuberculosis verrucosa cutis: x-rays, subintensive with filtration.

3. Scrofuloderma: x-rays, subintensive with filtration.

4. Erythema induratum: x-rays with filtration.

Verrucous Lesions.—1. Verruca vulgaris: x-rays, 350 roentgens, can be repeated at end of five weeks; protect normal surrounding skin.

2. Verruca plantaris: x-rays, 350 roentgens; radium.

3. Cornu: x-rays, 350 roentgens; must remove the cause.

4. Keratosis: radium.

Malignant New Growths.—1. Basal cell epithelioma: x-rays, 350 to 1400 roentgens.

2. Prickle cell epithelioma: x-rays, 350 to 2400 roentgens, plus infiltration.

RADIUM

Types of Rays and Their Uses

Radium emits three kinds of rays: *alpha*, *beta* and *gamma*, each with its own property. In the process of disintegration of the radium atom several products are formed, notably helium, and the provisionally named radium A, radium B, radium C, radium D and radium E. The beta and gamma rays are used for therapy and both originate in neither radium nor radon but in the decomposition products, radium B and radium C. Alpha rays have no therapeutic value as they are readily absorbed by a sheet of ordinary writing paper or a sheet of rubber. Beta rays penetrate only a few millimeters of tissue, which limits their therapeutic value to extremely superficial diseases. Deep lesions are treated with gamma rays by eliminating the beta rays with a filter to lessen the reaction of the superficial tissues.

Factors Determining Method of Application

The thickness and location of the lesion to be treated regulate the method of radiation application. Superficial dermatoses require beta radiation. Lesions that are thicker but still superficial require the removal of the softest beta rays

with a filter (0.1 mm. of aluminum). Lesions that are 3 to 4 mm. thick require a filter that will give almost pure gamma radiation (2 mm. of brass). A recent tendency to increased screening is growing in favor with dermatologists. Screened applicators require a longer period of time than unscreened applicators.

The distance of the radium from the surface of the skin is increased according to the depth of the lesion to be treated. The increase of distance between the radium and the lesion lessens the intensity coming from the source and follows the law of inverse squares.

Radium Applicators

Radium applicators are made in four standard designs: tubes, needles, implants, plaques.

Tubes of various sizes are used as containers of radium salt. They are used upon the surface of the skin, inserted into cavities or interstitially. The amount of radium sulfate contained in a tube ranges from 5 to 25 mg.

Needles made of platinum are used in interstitial therapy or enclosed in containers and used externally.

Implants are made of platinum, and are designed for use where it may be objectionable to leave a foreign body permanently imbedded in tissue.

The limited use in dermatology of tubes, needles and implants makes it impossible to discuss their therapeutic uses, but some space must be devoted to the type of applicator used most frequently by dermatologists.

Most American dermatologists use radium *plaques*. Three strengths of radium plaques are in use: half strength, containing 2.5 mg. of radium per square centimeter of active surface; full strength, 5 mg. per square centimeter; double strength, 10 mg. per square centimeter.

One full strength plaque containing 10 mg., of radium element to 2 sq. cm. (1.4 by 1.4 cm.) can be used to advantage for most conditions in dermatology. Such a plaque should be provided with an aluminum screen of 0.1 to 0.2 mm. thickness to remove the soft rays, and with a brass filter of 2 mm. thickness to provide gamma rays. It is advisable to

become familiar with a few screens and know their therapeutic values and limitations. Next it is necessary to know the erythema dose of the radium plaque. The exposure time required for an erythema dose with a full strength plaque is about five minutes. Begin with an exposure time below that which will produce a reaction. If this does not show redness at the end of ten days, increase the time on the next exposure. Make these tests on your skin and several other persons. After the dose for the unfiltered plaque is found, then establish it for the aluminum filter, and last for the brass filter.

Diseases Treated with Radium Plaques

Nevus Vasculosus.—Nevus vasculosus (strawberry mark) is a type of angioma in which good results follow radium treatment. It is a lesion of variable size and shape, slightly elevated, reddish, occurring on the face, neck, head, arms, although no region is exempt; it is permanent or disappears spontaneously, leaving white or pigmented atrophic scars.

The effect of beta rays of radium is more successful than other methods of treatment, and without discomfort to the patient. Several treatments will usually cause the lesion to disappear.

A radium plaque, full strength, screened with 0.1 mm. of aluminum, with an exposure time of eight to ten minutes is needed. Reactions should be avoided and the treatment is repeated at the end of every five weeks until the angioma has disappeared. The lesions should be shielded closely. Treatment should be started early, since nevi are then more radio-sensitive than later in life.

Angioma Caverosum.—This lesion consists of a soft tumor with involvement of the deep veins. It may or may not undergo spontaneous involution, which is one reason for conservative treatment.

Beta rays of radium are indicated in the superficial type and the deeper lesions are treated with gamma rays of radium. The filtration and exposure time are similar to those for the strawberry mark, depending upon the size and depth. Again, treatment should be started in infancy. Large and deep-

seated cavernous angiomas should be treated with gamma rays of radium. A full strength plaque with 2 mm. of brass for filtration may be used in contact three and a half hours.

Basal Cell Epithelioma.—Theoretically, the results of treatment of basal cell epithelioma should be similar with radium and x-ray. In certain regions the lesions are more accessible to radium therapy. Radium screened to produce beta rays is successful for many superficial lesions. A full strength radium plaque screened with 0.1 mm. of aluminum is placed in contact with the lesions for thirty to forty-five minutes. Thicker lesions, more than 2 mm., are treated with gamma rays. A full strength plaque screened with 2 mm. of brass and 0.1 mm. of aluminum is placed in direct contact with the tumor for four to nine hours.

Dermatitis Papillaris Capillitii (Acne Keloid).—This disease, which usually occurs on the neck and consists of follicular papules and pustules and ends in scarlike formations, resembling keloids, is successfully treated with radium with good results. The technic is similar to that employed for keloids.

Plantar Warts.—Plantar warts are successfully treated by various methods in some instances. Some warts are refractory to all known methods of treatment. A plaque can be conveniently used in the treatment of plantar warts after the horny layer is removed. An unscreened full strength plaque in contact with the wart, sharply screened, is used for fifteen to thirty minutes. Many times some of the remaining horny layer covering the wart absorbs the beta rays and then the gamma rays are effective, even though a filter is omitted.

Senile Keratoses.—The thin lesions of senile keratosis are treated successfully with beta rays, and a full strength plaque screened with 0.1 mm. of aluminum can be applied for thirty minutes. Many superficial ones are treated with a full strength plaque, unscreened, for fifteen to eighteen minutes.

Leukoplakia.—MacKee states that the first recorded instance of the treatment of leukoplakia with x-rays was by Pusey in 1904. I cannot do better than to give Pusey's treatment of leukoplakia which I carried out many times from

1921 to 1940. Until 1930 many of the smaller areas of leukoplakia were treated with beta rays, as I still remember some of the cases in which I held the radium in contact with the lesion. A few were helped, at least for a time, but recurrence followed. Some of the patients never returned, so the results are not known. Extensive areas of leukoplakia were never treated with radium but were given one-half strength Dobell's solution, a favorite mouth wash used by Pusey for many diseases of the mouth. I remember cases of leukoplakia and syphilis, but he never believed that syphilis was the cause of the leukoplakia. During the last ten years his attitude toward leukoplakia changed completely. It was a routine to keep patients with leukoplakia under observation, if possible, and if signs of malignancy appeared to treat it with radium or by surgical removal. I do know that leukoplakia was never treated with x-rays by Pusey after 1930. Pusey never shared with many physicians and dentists the view that leukoplakia was usually precancerous. He believed that a certain number of patients were to have cancer of the mouth, regardless of the leukoplakia.

Keloids and Hypertrophic Scars.—These conditions are neglected by many physicians. Hypertrophic scars following injury are common enough to warrant a few words about their treatment. The differences between keloids or hypertrophic scars are not significant, as the method of treatment is the same for both. My choice between radium and x-rays is determined by the factor of convenience. The results are alike. Routinely for all keloids that are superficial the soft beta rays are eliminated with a 0.1 mm. of aluminum. Direct contact with this screening requires ten to eighteen minutes for a full strength plaque. Gamma rays are required when the lesion is more than 2 mm. thick. A full strength plaque screened with 2 mm. of brass and 2.4 mm. of rubber is placed in direct contact with the hypertrophic scar for four to eight hours.

The type, size and strength of the applicator, exposure time, distance from the skin, and thickness of the filter and its composition are important factors in the therapeutic use of radium.

Radon

Radium and radon are chemical elements, the first being a solid and the second a colorless gas. Radon is like radium in that it has the uncontrollable property of spontaneous disintegration. Space does not permit a description of the collection and purification of radon. The reader is referred to MacKee's textbook for this and a series of tables for computing its strength under various conditions.

The dermatologist finds the greatest use for radon in interstitial irradiation. Radon is usually contained in small gold capillary tubes having a wall thickness of 0.3 mm., length of 4 mm., and an external diameter of 0.75 mm. when prepared.

Gold seeds (wall thickness 0.3 mm.) give off 91 per cent gamma rays and 9 per cent beta rays. The gold seeds are inserted with a trocar.

Radon is implanted in the tissues and left *in situ*. This has the advantage of distributing the radiation equally to the lesion, provided 1 millicurie seed is placed into 1 cc. tissue. If ulcerating surfaces are present the seeds are implanted near the edges of the growth to prevent the carrying of infection deeper. The number of gold seeds required and their contents depend upon the size and depth of the growth.

RADIOTHERAPY DAMAGE TO THE SKIN

If radium and x-ray are used beyond the toleration point of the skin, either at one or more exposures, the cumulative effect results in injury such as atrophy, telangiectasia, keratosis and cancer. This occurs less frequently now in the radiotherapy of cutaneous disease than it did in former years. However, such injuries are on the increase following deep radiotherapy. They will continue because the radiotherapist is primarily concerned with the treatment of deeper structures rather than the skin. He forgets about the intervening skin that tolerates only a given amount of radiation which is usually less than the toleration of the deep-seated lesion.

Only a few diseases of the skin require a definite erythematous reaction and they are the malignant conditions. The majority of the diseases of the skin seldom require a visible

reaction. A mild erythema produced by radiotherapy may result in objectionable sequelae.

Factors Contributing to Skin Damage

Irritating *local remedies* are never used in conjunction with radiotherapy as they may decrease the toleration of the skin. The *age* of the patient should be considered before using radiotherapy as the younger patient tolerates less radiation than an older person. The *color of the skin* should be considered, as a darker skin tolerates radiation better than a light skin. Also there are variations in the skin depending upon the region radiated. *Overlapping* of the areas treated may cause trouble. It is a good plan to protect the normal skin with sufficient lead masks to prevent damage. A mistake that often causes damage is the omission of a *filter* when one was intended, but the use of a filter is seldom indicated in most of the dermatoses that are treated with x-rays.

BIBLIOGRAPHY

1. MacKee, George M.: X-rays and Radium in the Treatment of Diseases of the Skin. Third Edition. Lea & Febiger, Philadelphia, 1938.

TOXIC DERMATOSES

MAX S. WIEN, M.D.*

THAT certain dermatoses are of toxic origin is well established. Eruptive lesions of varied character may follow the ingestion of certain foods or drugs in some individuals. The frequency of drug eruptions has greatly increased in the past decade with the introduction of a large number of new synthetic drugs to the therapeutic armamentarium of the physician. The coal tar derivatives, serums and sulfonamides are well recognized by most practitioners as being capable of producing toxic eruptions in certain persons.

ETIOLOGY OF THE ERYTHEMA GROUP OF SKIN DISEASES

In the clinic today, in addition to the aspects mentioned, I shall discuss toxic eruptions in their broadest aspects, including allusion to the broad concept of the toxic erythema group of dermatoses discussed by Osler,¹ when he stressed the occurrence of certain eruptions that were related to vascular lesions. These eruptions are sometimes associated with joint pains and exceptionally with effusion in and about the joint. In a small proportion of cases the mucous membrane of the mouth is also affected. It is very important that practitioners recognize that certain cutaneous eruptions, in many instances, are visible morphologic manifestations that are intimately related to certain underlying constitutional conditions. By cataloging these eruptions properly and by recognizing their role in visceral diseases, this visible link (in the skin) can be readily utilized as a diagnostic aid. With a full appreciation of this enlarged concept in medicine, the taunt of some medical practitioners "that dermatology is a

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specialty with long names and conditions that are treated with calamine lotion" will cease to "hold water."

Engman and Weiss,² in an excellent discussion on "The Erythema Group of Skin Diseases," said: "There undoubtedly exists a close clinical, pathologic and etiologic relationship between the following conditions: urticaria, erythema multiforme, dermatitis herpetiformis, pemphigus, purpura and certain types of cutaneous gangrene. These so-called clinical entities should probably be included in one group on account of the fact that various etiologic factors may cause the same type of these eruptions or any one etiologic factor may cause varied types of these eruptions. It is also highly probable that certain types of lupus erythematosus disseminatus and the scarlatiniform or toxic erythemas should be included."

They state that "we are indebted to Osler for the best point of view of this group of diseases, as he has shown its *relation to general medicine, and that the cutaneous symptoms are, in many cases, only a symptom of various constitutional conditions or diseases of the internal organs.* However, attention had previously been called to the apparent relationship by Gilbert, Rayer, Besnier and Doyon, and others, but not so forcibly as in the masterly series of articles by Osler."

The data from Engman and Weiss, given in Table 1, on the etiology of the erythema group, will indicate to the practitioner the extent and diverse character of the etiologic agents in the production of cutaneous efflorescences that may be dependent upon the action of noxious agents on the vascular endothelium at the affected site.

It will be seen that under the head of "Eruptions of Toxic Origin" are a vast number of cutaneous entities, some of which are manifestations of the vascular injury due to food, micro-organisms, serums or vaccines in diseases of the viscera,¹ and another group that may be due to the ingestion or injection of certain drugs. The acute exanthemata are not included because they are characterized by such well marked common features as a definite course and general constitutional disturbances that they form an easily separable group and are well recognized by all. The toxic eruptions of which

I shall speak are those due to drugs and certain eruptions for which we are usually unable to ascribe a definite cause but which we know are caused by toxins and deserve a place in the group of toxic eruptions, *e.g.*, urticaria, purpura and erythema nodosum.

TABLE 1

ETIOLOGY OF THE ERYTHEMA GROUP²

Internal origin	Foods			
	Helminths			
	Disease of the internal organs.....	{	Endocrine	
			Liver	
			Kidney	
			Lungs	
	Drugs	{	Pleura	Arthritis
			Uterus	Vaccinia
	Serums	{	Foci	Pyorrhea, etc.
	Vaccines	{		Nasal
	Burns	{		Tonsil
				Urethra
	Micro-organisms	{	Micro-organisms	Visceral
				Typhoid
				Rheumatism
				Syphilis
		{		Malaria
				Streptococci
				Exanthemata
				Other unknown organisms
		{	Toxins	Diphtheria
				Tetanus
				Botulism
				Plague
	Pregnancy			Pyocyaneus
	Hydatid	{	Involution	Other unknown organisms
	New growths			
	Breaking down of pathological tissue			
				Radiotherapy

DRUG ERUPTIONS

A number of eruptions are produced in susceptible persons by absorption and hematogenous spread of a drug or its split product following ingestion or injection of the drug.³ In

TABLE 2

MORPHOLOGIC CLASSIFICATION OF DRUG ERUPTIONS, WITH CAUSAL DRUGS
(after MacLeod)

<i>Erythematous eruptions</i>	
Papular..	Antipyrine; belladonna; bismuth; chloralamide; copaiba; cubebs; gold; iodides; phenacetin, etc.
Macular and patchy..	Animal serum; antipyrine; arsenic; belladonna; bismuth; bromides; chloral; chloralamide; copaiba; cubebs; gold; iodides; morphine; opium; phenacetin; potassium chlorate; quinine; salicylates; turpentine.
Morbilliform .	Animal serum; antipyrine; arsenic; belladonna; copaiba; cubebs; luminal; sulfonal; turpentine; sulfanilamide.
Scarlatiniform	Animal serum; antipyrine; arsenic; belladonna; chloral; copaiba; cubebs; hyoscyamus; luminal; opium; pilocarpine; sulfonal; turpentine.
<i>Exfoliative dermatitis</i>	
Secondary erythrodermia	Chrysarobin and derivatives and tar externally; arsenic and gold by injection; luminal and sulfanilamide.
<i>Urticarial eruptions..</i>	
	Animal serum; arsenic; bromides; copaiba; cubebs; iodides; luminal; mercury; opium; phenacetin; phenolphthalein; quinine; salicylate of sodium; santonin; turpentine, etc.; sulfonamides.
<i>Vesicular eruptions.</i>	
	Antimony; antipyrine; arsenic; bromides; chloral; copaiba; gold; iodides; phenolphthalein; quinine; turpentine; etc.
<i>Herpetic eruptions</i>	
(Herpes zoster or Herpes simplex)..	Arsenic.
<i>Bullous eruptions.</i>	
	Antipyrine; bromides; chloral; iodides; opium; quinine; salicylates; sulfanilamide; etc.
<i>Polyomorphic eruptions of the erythema multiforme type</i>	
	Animal serum; antipyrine; chloral; copaiba; cubebs; iodides; opium; potassium chlorate; etc.
<i>Pustular eruptions</i>	
	Antimony; antipyrine; arsenic; bromides; iodides; opium; salicylates; turpentine. (Of these the most common causes are bromides and iodides.)
<i>Acneform</i>	
	Antipyrine; arsenic; bromides, chloral, iodides, opium.
<i>Ulcerative.</i>	
Condylomatous or Anthracoid	Arsenic; bromides; chloral hydrate, iodides.
Gangrenous.	Arsenic; iodides; quinine.
<i>Purpuric and petechial eruptions.</i>	
	Animal serum; antipyrine; bromides; copaiba, ergot; iodides, potassium chlorate; quinine; salicylates; sulfonal, sulfathiazole, estrogenic substances.
<i>Keratotic eruptions</i>	
	Arsenic, bismuth.
<i>Pigmented eruptions</i>	
	Arsenic, gold, silver nitrate, phenolphthalein

some cases there appears to be an idiosyncrasy and small doses will produce an eruption. while in others large doses or administration of the drug over a prolonged period

(cumulative effect) are necessary before the eruption appears. The skin eruption may at times be the only symptom but it is also often accompanied by mucosal lesions and by constitutional symptoms, e.g., headache, nausea, vomiting and diarrhea.

Drug eruptions most commonly involve the trunk and extremities and are usually generalized, profuse and symmetrical, with a predilection for the dependent portions of the body. Table 2 indicates the morphologic characteristics of certain drug eruptions, and enumerates some of the causal drugs.

Phenolphthalein

Some years ago I saw an Indiana physician, aged fifty years, who had had recurring attacks of coin size, polychromatic, ecchymotic lesions on the trunk and extremities. After a very thorough "going over" by his colleagues at home and the finding of cloudy sinuses on the x-ray plates, they had decided he had erythema multiforme with sinus infection as the focus. The consulting otolaryngologist to whom he was referred did not feel that there was enough evidence of sinus infection to warrant radical operative treatment of his sinuses and referred him to me for an opinion regarding the skin lesions.

In any case of drug eruption when the index of suspicion of a drug as the causal agent is high, based upon one's knowledge that a certain morphologic picture in the skin is often due to the ingestion of certain drugs, it becomes necessary for the physician to assume the role of a detective and question his patient very carefully regarding the ingestion of any type of drug and particularly certain proprietaries. Unfortunately, many patients do not look upon pills or tablets taken for constipation as medicine and, since many of these proprietaries contain phenolphthalein¹ and this drug is capable of producing a characteristic eruption in the skin, one must check and re-check the history of drug ingestion with the patient.

Upon close questioning of the patient under consideration, it was found that he had been in the habit of pouring phenol-

phthalein powder into the palm of his hand and then taking up these unmeasured doses with his tongue and swallowing them with a draught of water. He had been doing this for a long period of time. When it was pointed out to him that the eruption he presented was compatible with that produced by phenolphthalein and was most probably related to drug ingestion rather than a focus of infection in his sinuses, he recalled a definite "time relation" between the cutaneous efflorescence and the ingestion of phenolphthalein. The eruption cleared when the phenolphthalein was discontinued. Later a colleague in St. Louis informed me that the patient had consulted him concerning a recurrence that came on shortly after the further ingestion of phenolphthalein for constipation.

I wish to re-emphasize the need for *questioning* and *re-questioning* with great patience any individual in whom you suspect a drug eruption. This patient fulfilled the criteria for diagnosis of a drug eruption, viz., improvement on withdrawal of the drug and a flare-up or recurrence of the eruption upon the re-ingestion of the drug.

Bromides

A woman, aged forty-seven years, had been suffering with nervousness and insomnia for a period of weeks, for which she consulted a physician who prescribed a medicine internally. She subsequently developed furunculoid nodules over the tibiae. Another physician was called, after the skin eruption appeared, who suspected pemphigus and asked for dermatologic consultation. When first seen by me the patient presented erythematous nodular lesions on the lower extremities. When questioned about drug ingestion she stated that *she had taken no medicine except a sedative for the past six weeks*. On checking this sedative we found it contained bromides (Syrupus bromidorum, N.F.) and the cutaneous eruption fitted into the picture of a bromide eruption and bore a definite time relation to the previous ingestion of the medicament. On withdrawal of this sedative and the administration of fluids and sodium chloride, the eruption cleared.

Barbiturates

A white man, aged forty-eight years, had been operated upon for ureteral stone. He received a barbiturate for post-operative insomnia and shortly afterwards developed a generalized erythematous eruption, with the greatest involvement on the dependent portions of the body. The eruption promptly cleared on withdrawal of the drug.

Sulfonamide Group

The literature is full of reports of varied cutaneous eruptions^{5, 7} resulting from the wide use of the excellent chemotherapeutic agents in the sulfonamide group, and I have emphasized in a recent article⁵ the need for recognizing these cutaneous manifestations in order to give security in the prescribing of these valuable drugs and prevent baneful effects from their use by early recognition of the toxic manifestations.

URTICARIA

The eruption known as urticaria, or "hives," which is due to a variety of causes, is well known to all of you. The characteristic wheal, which in most instances is the only essential lesion, appears rapidly, may or may not be associated with erythema and is usually associated with severe itching. The condition is frequently self-diagnosed by the patient, who will come in and say, "Doctor, I have the 'hives' which I believe are due to some strawberries or shellfish I ate yesterday." With this history, where there is a characteristic eruption and a definite time relation between the ingestion of some unusual article of diet and the appearance of the eruption--and in some cases associated gastro-intestinal distress--the diagnosis is easy and it is only necessary for the physician to institute the proper topical and internal therapy to alleviate the condition which, as a rule, promptly subsides.

In certain chronic urticarias the problem is more complicated and bowel infection⁶ and the emotions⁸ must be investigated and ruled out as causal agents. Drugs, *e.g.*, aspirin and the sulfonamides, may also be responsible.

PURPURA

Purpura is included in the broad conception of the erythema group;² it is an eruption of reddish or purplish spots due to multiple nodular hemorrhages into the skin or mucous membranes. Purpura is a physical sign and not a disease, and may occur in a large number of conditions as revealed by Table 3.

TABLE 3

PURPURA: TYPES AND ETIOLOGIC FACTORS (from Tidy, slightly modified)

Primary Purpura

- | | |
|----------------------|----------------------|
| Purpura simplex | } Arthritic purpuras |
| Purpura rheumatica | |
| Henoch's purpura | |
| Purpura hemorrhagica | |
| Purpura fulminans | |

For details of these diseases a textbook of medicine should be consulted.

Secondary and Symptomatic Purpura

- | | |
|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Specific infectious fevers. . | . Typhus, always.
Smallpox, frequently.
Cerebrospinal meningitis, frequently.
Scarlet fever, in severe cases.
Measles, in severe cases.
Typhoid fever, rarely.
Other diseases, occasionally. |
| 2. Septic infections. | Infective endocarditis, frequently.
Septicemia.
Pyemia. |
| 3. Blood diseases . . . | Leukemia, especially the acute form.
Aplastic anemia.
Pernicious anemia, rarely. |
| 4. Toxic conditions . | Snake poison; serums. |
| 5. Drugs, etc.. | Chloral; copaiba, quinine; belladonna; iodides; nitroglycerin; neosalvarsan, rarely
Sulfonamides, occasionally. <i>Estrogens</i> . ¹² |
| 6. Constitutional and cachectic conditions | Scurvy; chronic nephritis; carcinoma; tuberculosis; old age. |
| 7. Severe jaundice from any cause | Tabes, peripheral neuritis, hysteria. |
| 8. Nervous diseases, rarely . | Venous stasis, due to tight bandages; varicose veins; failing compensation in heart disease; on first standing up after long illness; paroxysms of whooping cough or epileptic attack. |
| 9. Mechanical causes | |
| 10. Allergy in relation to purpura. ¹³ | |

In evaluating the purpuras it is important to include the severe hemorrhagic types, acute specific fevers, drug ingestion or injection, scurvy, infectious endocarditis, and blood dyscrasias.

ERYTHEMA NODOSUM

Erythema nodosum may occur as a definite affection with the appearance of subcutaneous nodules, which are usually symmetrical, and distributed over the legs anteriorly. The nodules are red and painful and may have the varied color changes of a bruise and may come out in crops. They never ulcerate or break down, and may occur as part of the erythema group of skin diseases.²

Erythema nodosum-like lesions may also be produced by micro-organisms^{10b} and by drugs⁷ and are occasionally seen in association with lymphogranuloma inguinale.^{10a} In adults⁹ the condition is commonly associated with rheumatoid pains. Its association with rheumatoid symptoms has been discussed by Skiold,⁹ who in a study of 128 adults with erythema nodosum found 21 per cent who showed symptoms and signs of arthritis. A concomitant rheumatoid involvement of the heart was demonstrated in two patients. Erythema nodosum has also been described as a toxic eruption from the use of sulfonamides.⁷

Erythema nodosum may occur, especially in children, as part of a toxic eruption due to the bacillus of tuberculosis (tuberculid).

TUBERCULIDS

Cutaneous tuberculosis is of great importance to practitioners as a link between dermatology and general medicine. I want to emphasize the importance of recognizing the morphology of skin eruptions that may be cutaneous manifestations of a toxic reaction to a latent or manifest focus of tuberculosis in the system and to urge you to make diligent clinical and laboratory investigation for a focus of tuberculosis in any patient presenting tuberculid-like lesions. When tuberculosis is present, these lesions are spontaneous examples of Koch's phenomenon resulting from endogenous inoculation of the skin. Lack of time precludes my discussing in detail the more than twenty-two cutaneous entities, listed by Senear,¹¹ which may or may not relate to an underlying tuberculosis. Their presence, at least, should make the practitioner suspect the presence of a latent or manifest focus of

tuberculosis until he has completely ruled it out by proper clinical and laboratory examination.

Examples are given in Table 4 of tuberculid and other lesions which require differentiation. I suggest that you refer to any of the standard textbooks on dermatology for a detailed discussion of these entities so that you may be familiar with their pictures.

TABLE 4¹¹

TUBERCULID AND OTHER SKIN LESIONS WHICH REQUIRE DIFFERENTIATION

Lichen scrofulosorum	Lupus pernio
Papulonecrotic tuberculids	Lupus erythematosus ^{2, 11}
(a) Acnitis	Lichen nitidus
(b) Folliclis	Granuloma annulare
Erythema induratum	Angiokeratoma (Mibelli)
Acne scrofulosorum	Pityriasis rubra (Hebra)
Acne varioliformis	Pityriasis rubra pilaris
Acne cachecticorum	Erythema nodosum
Sarcoids	Erythema multiforme
(a) Multiple benign sarcoids of Boeck	Purpura
(b) Subcutaneous sarcoids of Darier-Roussy	Parapsoriasis
(c) Erythema induratum-like sarcoids of the extremities	Eczema scrofulosorum

You will note that *erythema nodosum* is in the above list, and in children the occurrence of erythema nodosum must be given particular attention since it often represents a spontaneous example of Koch's phenomenon resulting from endogenous inoculation of the skin.

The incidence of tuberculosis in children with erythema nodosum is so high that some writers have concluded that it represents active invasion of the skin by the tubercle bacilli or its toxin, and might be a prodromal sign of an acute tuberculous septicemia and terminate in a fatal meningitis.

BIBLIOGRAPHY

1. Osler, Sir William: Brit. J. Dermat., 12: 227, 1900, and Amer. J. Med. Sc., Vol. 127, 1904.
2. Engman, M. R. and Weiss, R. S.: The Erythema Group of Skin Diseases. Arch. Derm. & Syph., 12: 325 (Sept.) 1925.
3. Loveman, A. B.: Allergic Drug Eruptions. J. Allergy, 11: 48 (Nov.) 1939.
4. Belote, G. H. and Whitney, H. K.: Phenolphthalein Compounds. Arch. Derm. & Syph., 36: 279 (Aug.) 1937.
5. Wien, M. S. and Lieberthal, E. P.: Pemphigus Foliaceus-like Toxic Reaction Following Sulfonamides. J.A.M.A., 117: 850 (Sept. 6) 1941.

6. Traut, Eugene F.: Management of Intractable Urticaria. *Arch. Derm. & Syph.*, 40: 368 (Sept.) 1939.
7. Volini, I. F., Levitt, S. O. and O'Neil, H.: Cutaneous and Conjunctival Manifestations of Sulfathiazole Intoxication. *J.A.M.A.*, 116: 938 (Mar. 8) 1941.
8. Stokes, John H.: Psychoneurogenous Reactions of the Skin. *Arch. Derm. & Syph.*, 42: 780 (Nov.) 1940.
9. Skjold, N.: Rheumatic Symptoms in Patients with Erythema Nodosum. *Nord. med. tidskr.*, 15: 595 (Apr. 15) 1938.
- 10a. Wien, M. S.: Lymphogranuloma Inguinale. In *Modern Urology* (Cabor), Lea & Febiger, Philadelphia, 1936, Vol. 1, p. 234.
- 10b. Jadassohn, Samek and Fischer, Ulcus Vulvae Acutum Associated with Lesions of the Mouth. Quoted by Wien, M. S. and Perlstein, M. O. in *J.A.M.A.*, 95: 471 (Feb. 6) 1932.
11. Senear, Francis E.: The Importance of the Tuberculides in Medical Diagnosis. *Contributions to Medical Science, Dedicated to Alfred Scott Warthin*, 1927, pp. 319-331.
12. Loftis, E. L.: Purpura Due to Injection of Estrogenic Substance. *Arch. Derm. & Syph.*, 42: 138 (July) 1940.
13. Thomas, J. W. and Forsythe, J. R.: Allergy in Relation to Purpura. *J. Lab. & Clin. Med.*, 26: 1105 (April) 1941.
14. Symposium on Lupus Erythematosus. *Proc. Staff Meet. Mayo Clin.*, Vol. 15, No. 43.

SUPERFICIAL FUNGOUS INFECTIONS

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Importance of Accurate Diagnosis.—The increasingly frequent occurrence of superficial fungous infections (so-called "ringworm") of the skin, especially the eczematoid type of eruption of the hands, demands a more exacting diagnostic approach because of the confusion with many other similar skin infections and irritations. The ever-increasing number of vesicular and oozing eruptions of the fingers demands a clinical and laboratory appraisal that is as accurate as can possibly be given, not only to secure quick results from treatment but also to prevent the use of overly strong preparations which might turn a mild dermatitis into a recalcitrant condition requiring long therapy.

RINGWORM OF THE HANDS AND FEET: DIFFERENTIAL DIAGNOSIS AND TREATMENT

Ringworm of Feet with Toxic Eruption on Hands

Today we have a young man of twenty-one years, a college student who, you see, has small vesicles on the sides of the fingers of both hands. They are of three days' duration, and are accompanied by considerable itching. Dermatologic examination reveals minute vesicles constituting a symmetrical eruption of all the fingers of both hands. An occasional vesicle is present on the palmar surfaces. Further examination reveals no other lesions on the body but there are present eroded areas between the toes of both feet, especially in the fourth interspaces. On questioning the young man we find that he has had "sores" on his feet for a number of years, especially pronounced during the hot weather and disappearing almost completely at other times of the year.

Diagnosis.—To make an accurate diagnosis it is desirable to take small pieces of the eroded area, place them in 10 per

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cent *potassium hydroxide* and put in a moist Petri dish for at least forty-eight hours. Examination of these pieces of skin under the low power microscope reveals the hyphae of fungi which are responsible for the condition generally called "ringworm." While it is usually easy to find the fungi under the microscope, low power, many laboratory workers have recently been staining suspected tissue to confirm their presence and to identify the variety. Schubert has done a great deal along this line and has found that the method of Swartz and Conant is the most practical one, the stain consisting mainly of the Porrier blue (0.25 per cent).

Clinically and microscopically, then, we have a fungous infection of the feet. These interdigital lesions of the feet are readily diagnosed clinically by their localization in these areas, where they are oftentimes accompanied by deep-seated vesicles and bullae on the plantar surfaces. It is readily appreciated that few practitioners are experienced in the laboratory study of fungi, but the simple potassium hydroxide test as described should be a part of a working knowledge of every physician who handles this type of case. This simple examination will decrease the diagnostic confusion which arises in many of these cases, and is of particular value in the differentiation of suspected industrial irritations where it is important to have an accurate diagnosis.

The staining of cutaneous fungi for diagnostic purposes is still in its infancy. At the present time the procedure is not suited to ordinary practice but I mention it to illustrate the fact that laboratory workers are on the alert to help the clinicians in diagnosis.

The vesicular eruption on the hands of this patient is a toxic manifestation of an active focus of infection on the feet. The symmetry of the lesions on the hand and their appearance following an acute exacerbation of the lesions on the feet make almost certain that the condition is a toxic eruption of the fingers resulting from a distant focus of active ringworm infection.

Treatment.—The therapeutic management of this type of lesion will be discussed more in detail later; suffice it to say at this point that the eruption on the hands should never be

treated with strong preparations of any type. Soothing therapy should be instituted and the active measures used upon the active focus in the feet.

Allergic Dermatitis of Hands and Feet Simulating Ringworm

The patient, a woman aged twenty-eight years, has a grouped vesicular fissured lesion of the small finger of the right hand and a similar lesion on the distal phalanx, dorsal surface of the third finger of the left hand. She states that blisters have appeared on the backs of the toes simultaneously with the lesions on the hands. She has never before had an eruption of this type, but states that as a baby she had "eczema" of the antecubital surfaces. Furthermore, she has hay fever during the usual hay fever season, August and September, and states that she believes she is sensitive to ragweed pollen though no skin tests have ever been performed.

Diagnosis.—Dermatologic examination reveals an erythematous vesicular fissured area on the two fingers as mentioned and similar lesions on the dorsum of each large toe. The appearance of these lesions immediately suggests a fungous infection, but repeated potassium hydroxide preparations under the microscope reveal no fungi. It is well known that, unless we find the fungi on microscopic examination, a culture grown on Sabouraud's media is seldom positive; hence, the immediate microscopic examination is the most important. We can now see that these lesions are on the dorsa of the toes and there are no sodden areas between the toes and no deep-seated vesicles on the plantar surfaces. Thus, clinically, we do not have any evidence of a superficial fungous infection.

Clinically, then, this is a vesicular eruption with an allergic background that during the pollen season could easily be due to the inhalation of a pollen to which the patient is sensitive. It cannot be emphasized too strongly that there is no ringworm basis in cases of this type.

Treatment.—Soothing therapy is indicated and then a thorough allergic study should be made. If the patient is found to be allergic to active pollens, proper desensitization therapy should be instituted.

Contact Dermatitis (Possible Confusion with Ringworm)

Our next patient is a man in his early forties, who works in a plant where he is in contact with oils, greases, thinners and lacquers. He has been doing this type of work for several years and has occasionally noticed a "breaking out" on his hands during the extremely hot spells. He states that an eruption now present on his fingers and hands is of ten days' duration. This attack is so severe that he is unable to continue working at his usual task.

Diagnosis.—Dermatologic examination reveals an oozing, edematous eruption on all the fingers and on the backs of the hands, with a few erythematous areas on both wrists. Examination elsewhere gives negative results except for the finding of a few interdigital scales between the toes.

The intensity of the eruption on the hands is an almost certain indication that it is due to an external irritant—one that he probably is in contact with at his work or at home or in the garden. The few scaling areas between the toes clinically mean a mild fungous infection. It is well known that an active fungous infection between the toes occasionally lowers the threshold of resistance to the various contactants which the patient encounters. However, we have here such a severe swelling of the hands that this observation is probably of very little importance. We will apply soothing wet preparations to afford him some relief, and then study him thoroughly in an effort to determine the exact contactants. The wet dressings should be made with either 1:1000 aluminum subacetate solution or 1:4000 potassium permanganate solution, if pustules are detected. Sedatives will have to be used to control the severe subjective symptoms which accompany this type of eruption. The salicylates and bromides are the first choice.

Patch Tests.—Obviously the patient feels that the lesions are due to his work and this undoubtedly is the angle to be attacked first. We secure samples of the various possible irritants which he encounters, for the performance of the so-called "patch tests." A small amount of the suspected irritant, in this case oil, in the strength in which the patient is using it in his work, is placed on a small piece of cotton and applied

to the patient's back on an area which we think is normal skin, where it is securely fastened by adhesive tape. If the patient gives a history of being sensitive to adhesive tape then collodion must be used.

In the presence of such a severe eruption it is well to have the patient stay in the office for several hours, after application of the patch, owing to the possibility of getting a positive reaction within a relatively short time. At the end of twenty-four hours the areas are examined. A positive reaction varies from a mild erythematous area in those instances in which a mild antigen-like substance, such as feathers, has been used, to a large bullous eruption if the preparation is more or less irritating or if the patient is extremely sensitive to it. The value of the patch test is immediately questioned because the preparations are placed on a part of the skin which is not subject to the environment in which the patient works. Obviously we cannot place it on the parts which are already erupted for we could not detect any measure of intensity or any positive reaction.

The patient in question shows a reddened area of skin where the oil was placed and, consequently, we may assume that he is sensitive to this particular type of oil and that this is the most likely cause of, or the contributing cause to, the present eruption.

In other instances we find that the patient presents no positive patch reactions to irritants encountered in his work. Other things have to be considered, as a plant or vegetable poisoning acquired from working in the garden over the week-end or on a trip to the woods or a fishing expedition. Another possibility that must be kept in mind is that the lesion may be due, not to a contactant encountered in the work itself, but to one of various preparations used in the cleansing of the hands. Many soaps are irritating, and some workers even use the so-called thinners to cleanse their hands when this preparation is not used in their work at all.

"Emotional" Dermatitis of the Fingers

Our next patient is a man in his late forties who has had intermittent eruptions on his fingers for seven years. Dermatologic

examination reveals a number of small vesicles with an occasional fissure on the palmar surfaces of several of the fingers. It is an asymmetrical eruption and appears and disappears at intervals.

Diagnosis.—This type of case brings to mind immediately the possibility of a fungous infection, or so-called "dyshidrosis." On further study we find that the patient has not now, and never has had, an eruption on his feet. There is no allergic background. The eruption appears during various seasons, which would rule out the pompholyx we see during the summertime. Repeated studies for fungi are negative, so we can safely conclude that the dermatitis is not a primary fungous infection of the hands. Furthermore, there is no history of contactants and, after investigation along these lines, we can safely rule out that possibility. Thus by elimination, by the history and by detailed studies we can quite safely agree that this lesion is due to emotional factors, either of an exhaustion-fatigue type or just plain emotional instability due to financial worries, unsatisfactory home conditions, inability to accept responsibility, or an out-and-out neurogenous background.

In this type of case, much improvement can result from the attentions of a sympathetic neurologist. Only preparations of a soothing nature are to be used in such a syndrome.

Miscellaneous Infections of the Hands and Feet

Various other types of cutaneous lesions of the hands and feet may be seen in our clinic today and must be considered in the differential diagnosis of ringworm, although they are seldom encountered. For instance, occasionally we see *psoriasis*, at other times *lichen planus*, rarely *lupus erythematosus*, and sometimes a secondary *syphilid*. But these lesions are not eczematoid; that is, they are not characterized by blisters and do not ooze and do not come into a differential diagnosis in everyday practice. If there is doubt as to the real diagnosis, soothing applications like wet dressings of aluminum subacetate or a mild borated vaseline ointment can be used until a more accurate appraisal is secured.

Type of Fungi and Extracts

Before discussing detailed treatment I must mention that the type of fungi seen in cutaneous lesions is changing to some extent. A few years ago we almost always found *Epidermophyton inguinale*, but for the past ten or twelve years we have nearly always found the *Trichophyton interdigitale* and *gypseum* and occasionally *Monilia albicans*. In the past twelve to eighteen months we are again finding the *Epidermophyton inguinale*.

A few words might be said at this time on the diagnostic importance of the various biological extracts. We have used the polyvalent *trichophytin*, which is an extract of the various superficial invading ringworm fungi, and *moniliatin*, which is an extract of the *Monilia albicans*, in an attempt to solve our diagnostic difficulties. One-tenth of a cubic centimeter is injected intradermally in the flexor surfaces of the arm, and if there is a red raised area in twenty-four hours' time that is considered a positive test. We have found that most persons who react positively generally do have ringworm. In other cases in which there is a positive reaction, no fungus of any type is present superficially. It can be safely assumed that such a patient has had a fungous infection in the past or that a deeper fungous infection, such as *tinea sycosis*, has been present.

Treatment and Prophylaxis of Ringworm

Assuming now that a definite fungous infection of the feet is present, the type of treatment varies with the acuteness of the eruption. If there are large vesicles and bullae, with considerable erythematous reaction in the center of these, the infection must be treated like an acute dermatitis. *Wet dressings* as already described must be used for a few days, although I must hasten to add that occasionally we find a patient who is sensitive to potassium permanganate. Rarely we find that the wet dressings aggravate an acute condition and we must resort at once to soothing *dusting powders* and soothing *pastes*. A powder consisting of 5 per cent boric acid and 5 per cent sodium hyposulfite in equal parts of cornstarch

and zinc stearate is very efficacious during the day. At night, plain Lassar's paste can be applied to the areas that are not too large. The paste should be spread on gauze dressing as butter is spread on bread. If there is a marked toxic eruption on the body, such as large erythematous areas and obvious so-called mytid, a *soothing lotion* should be applied. One such lotion consisting of 10 per cent starch and 10 per cent zinc oxide in aqua calcis is of value in many of these cases. As already stated, mild *sedatives* must be used at times to control the subjective symptoms of burning and itching.

As the acute symptoms subside we encounter a whole encyclopedia of topical remedies for employment in the sub-acute and chronic stages. A few are of marked benefit, especially certain *paints* and our old-time *Whitfield's ointment*, to which either sulfur or ammoniated mercury can be added. An excellent paint mentioned by Pillsbury, which is applied at night, is made up of 1 per cent thymol and 5 per cent salicylic acid in 70 per cent alcohol. If the feet perspire a great deal an antiseptic powder can be used during the day, consisting of 5 per cent powdered camphor, 3 per cent salicylic acid, 10 per cent sodium bicarbonate and 20 per cent boric acid, in a talcum base. While a great many different preparations, such as ethyl iodide inhalations, copper iontophoresis, phenyl mercuric nitrate, and so on, have been on the market, our best results in most chronic cases come with the use of Whitfield's ointment or some modification of it.

In my opinion the most important factor in management is *accurate and proper diagnosis*, or an appraisal of all the factors entering into the individual case. In the hands of the expert, fractional *x-ray therapy* is at times of great help. As stated, the use of the biological extracts has proved to be of very little practical importance.

In the *prophylaxis* of ringworm sodium hypochlorite foot baths have proved effective in some instances. The patient, to prevent *recurrences*, must use the prescribed ointment or other preparation not only between the toes but around the nail edges, in order to kill the fungi which may lurk there and provide possible foci of infection.

OTHER SUPERFICIAL FUNGOUS INFECTIONS

While the superficial fungous infections, or so-called ringworm, of the hands and feet are the most common fungous infections of the skin, we occasionally find these fungi invading other parts of the body, and we have representative cases today of these various types of infection.

Tinea Cruris (Marginatum)

A young man, twenty years of age, presents an erythematous marginated eruption on each side of the groin of several weeks' duration. It is intensely pruritic and, according to the patient, it has extended very rapidly in the last few days. On examination we find a slightly elevated, marginated, erythematous, symmetrical eruption in the crural area. Examination of the other parts of the body reveals scaling, fissuring areas between the toes.

Diagnosis.—Clinically, then, we have here a typical case of tinea marginatum, often referred to as "jock-strap itch." While the appearance is typical, we can take scrapings for microscopic examination to confirm this clinical impression. As stated previously, the man in general practice is oftentimes unable to perform these laboratory procedures and ordinarily the clinical diagnosis is so typical that further laboratory procedures are unnecessary. Occasionally we find this same type of eruption in the axillae and at other times in the intermammary areas. When it involves the latter region we have to consider the possibility of a seborrheic dermatitis and occasionally psoriasis.

It is interesting to note that the present eruption is due to the *Epidermophyton inguinale*. This type of ringworm has been so rare in the past fifteen years that we have had difficulty in finding one case a year to show the medical students, but it has become very common in the past few months.

Treatment.—We can safely use the same preparations that are used for ringworm of the feet, but in about one-third the strength. As already stated, *Whitfield's ointment* in modified form is one of our best ointments. In addition, the *dusting powders* have been of great aid to us.

Moniliasis or Thrush

Occasionally we see the intertriginous areas of the intermammary and axillary regions infected by *Monilia albicans*, a yeastlike fungus of the thrush group. Here, of course, there is no involvement of the intertriginous regions of the feet, and in obese persons the possibility of glycosuria has to be entertained.

In the management, these particular infections respond much better to the *organic dyes*, as 5 per cent aqueous solution of gentian violet. In the acute phases the use of *wet dressings*, employing 10 per cent tannic acid, is especially efficacious.

Onychomycosis or Ringworm of Nails

Our next patient presents a disease of the fingernails of sixteen months' duration. She states that she first noticed some discoloration of the third finger of the left hand, and gradually it has involved practically all the other fingernails in asymmetrical progression. As we look at the nails we see that they are discolored in various gradations of black and brownish-black hues, and certain ones have the distal portions distinctly elevated. Distal to this elevation is a powdery débris from which we can take a scraping, which we examine under the low power microscope. Fungi are seen, so clinically and microscopically this is a typical ringworm of the nails, termed *onychomycosis*.

Differential Diagnosis.—Distal elevation of the nails with a powdery débris is typical of a fungous infection; the offending organism is usually the *Trichophyton gypseum*. In this type of syndrome the microscopic examination is of great importance, because *psoriasis* can oftentimes involve the nails and occasionally only the nails. The psoriatic nail is manifested either by a stippling, subungual opaqueness or by extensive erosion. Marshall Crawford of Boston has recently analyzed a large series of cases of psoriasis and finds that nail lesions were present in about half. Other nail dyscrasias which have to be differentiated are the *eczematous* changes, the *pyodermas*, the *onycholyses* as well as inflammatory *onychias* and *paronychias* due to other infections.

Treatment.—After the diagnosis is definitely established as ringworm of the nail, treatment is usually satisfactory in about three to four months' time. Local conservative measures consist first of the daily removal of all infected materials by scraping. After each scraping an ointment is applied, consisting of 10 per cent ammoniated mercury or 15 per cent sulfur precipitate in double-strength Whitfield's ointment. Occasionally a 5 per cent cinnabar preparation is very efficacious. Fractional *x-ray therapy* is of decided value in most cases. Surgical avulsion of the infected nails is *never* indicated because recurrence of the infection invariably follows this painful and debilitating procedure. In the occasional case in which the infection is due to the *favus* organism, treatment is very prolonged and sometimes ineffectual. These cases are very rare in the United States and Canada.

Ringworm of the Scalp

Our next patient is a boy eight years old who presents areas of alopecia on his scalp which his mother states are of two month's duration. As we examine the scalp superficially we see numerous areas with loss of hair, varying from a quarter of an inch to an inch in diameter. As we examine more closely we see no complete areas of alopecia, there being short stubs of hair here and there. Furthermore, numerous hair follicles in these patches have an erythematous zone around the hair root, through which a small pustule is protruding. In short, we are dealing with an inflammatory eruption, with loss of hair in a youngster below the age of puberty. Clinically this almost clinches the diagnosis of ringworm infection.

Differential Diagnosis.—In the differential diagnosis we have to think of *alopecia areata* and, in older people, of the rare cases of *folliculitis decalvans*. If one of the hairs is abstracted and placed in 40 per cent potassium hydroxide, we will find the fungi of the trichophyton group. In cases in which there is loss of scalp hair with a mild scaling eruption, then we will find *Microsporon audouini*, or the small-spored human ringworm.

It is interesting to mention here that tissues affected with fungi, and some other substances as well, give rise to a char-

acteristic fluorescent appearance when exposed to a beam of ultraviolet ray. An inexpensive glass filter, called the Wood filter, has been devised by Lewis and Hopper in this country. However, in ordinary practice these fine methods of diagnosis are unavailable and we must depend usually on the clinical appearance. Occasionally the trichophyton invades the beard, forming large pustular nodules, so-called *tinea barbae*. However, in this day of "streamlined" appearance the old-fashioned beard has disappeared, and consequently these eruptions are very seldom seen.

Treatment.—The choice of treatment lies between the use of local parasiticial preparations and x-ray in sufficient doses to produce epilation of the hair. The latter method has fallen into disuse owing to the possibility of errors in technic which produce a permanent alopecia. If epilation is necessary, manual removal is the method now advised. The use of *thallium acetate* orally to produce epilation is not advisable because of the possibility of serious constitutional reaction.

Topical applications are usually very efficacious, a 20 per cent sulfur ointment in petrolatum or a combination, such as 1 per cent each of iodine crystals, thymol and oil of cinnamon, being employed. An occasional ringworm of the scalp is caused by the *favus* organism. This is extremely resistant to all forms of treatment. Ringworm of the scalp in adults is practically unknown, although two cases were observed in the practice of Dr. Earl D. Osborne a number of years ago. Consequently, in the clinical diagnosis, ringworm of the scalp usually need not be considered in older patients unless they are in contact with livestock which may be infected.

CUTANEOUS DISEASES IN INFANTS AND CHILDREN

THEODORE CORNBLEET, M.D.*

SOMEBODY has said that the child is not merely a small person, but one with functions, capacities and attributes that differ in many respects from those of adults. His metabolism of protein and some minerals is somewhat different. His endocrinal make-up is different; his nervous and physical reactions in certain respects are different; and his skin is different. The latter is apt to be drier, to have hair less developed, to contain less pigment, to be thinner and finer in texture; and to have differences in secretion, as shown by the simple test of odor. The chemical make-up of his skin is different, as shown in its sodium-potassium ratio and water content. The response of the child's skin to irritants is somewhat different, tending toward vesicular reactions, whereas those of adults tend to be papular, lichenified and drier.

Because of all these differences, it is not surprising that certain skin diseases, such as *hydroa aestivale*, should occur characteristically in children. Some, as *lupus vulgaris*, often begin in childhood and having gained a foothold continue on into life. Still others, such as *nevi* and *xeroderma pigmentosum*, only seem to be characteristic of childhood, because they are either congenital and when seen later in life are taken for granted, or because they destroy the individual and so are not seen later. Of the substantial group of skin diseases which may be properly thought of in relation to children, space permits consideration of only several of them.

LICHEN URTICATUS

Lichen urticatus is also known as papular urticaria of childhood, though it is not entirely confined to children.

* Associate Professor of Dermatology, University of Illinois College of Medicine; Attending Dermatologist, Cook County and Mount Sinai Hospitals.

acteristic fluorescent appearance when exposed to a beam of ultraviolet ray. An inexpensive glass filter, called the Wood filter, has been devised by Lewis and Hopper in this country. However, in ordinary practice these fine methods of diagnosis are unavailable and we must depend usually on the clinical appearance. Occasionally the trichophyton invades the beard, forming large pustular nodules, so-called *tinea barbae*. However, in this day of "streamlined" appearance the old-fashioned beard has disappeared, and consequently these eruptions are very seldom seen.

Treatment.—The choice of treatment lies between the use of local parasitocidal preparations and *x-ray* in sufficient doses to produce epilation of the hair. The latter method has fallen into disuse owing to the possibility of errors in technic which produce a permanent alopecia. If epilation is necessary, manual removal is the method now advised. The use of *thallium acetate* orally to produce epilation is not advisable because of the possibility of serious constitutional reaction.

Topical applications are usually very efficacious, a 20 per cent sulfur ointment in petrolatum or a combination, such as 1 per cent each of iodine crystals, thymol and oil of cinnamon, being employed. An occasional ringworm of the scalp is caused by the *favus* organism. This is extremely resistant to all forms of treatment. Ringworm of the scalp in adults is practically unknown, although two cases were observed in the practice of Dr. Earl D. Osborne a number of years ago. Consequently, in the clinical diagnosis, ringworm of the scalp usually need not be considered in older patients unless they are in contact with livestock which may be infected.

CUTANEOUS DISEASES IN INFANTS AND CHILDREN

THEODORE CORNBLEET, M.D.*

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Urticaria is a form of allergy but the pathogenesis of lichen urticatus is unknown. Both display wheals at some time.

The lesions appear slowly in crops. When the physician first sees the patient there are already present fully evolved lesions. These are relatively hard, conical, discrete papules of flesh color or pinkish to reddish. They often appear puffy at the base, indicating their relation to wheals. These wheal-like lesions may be seen in pure form, at times interspersed amongst the other more numerous lesions, and are apparent especially at night. The papules evolve from wheals after the urticarial element disappears wholly or in part. Many of the lesions are excoriated and are capped by blood crusts. Excoriations appear at apparently uninvolved sites too, together with evidence of secondary infections with pyogens. In many cases the papules are dug out so that healing is followed by the formation of pitted scars. Rarely vesicles may be present, especially at the tips of the papules. In time some pigmentation develops at the favored sites, but there is no tendency to thickening of the skin or lichenification.

The extensor surfaces of both upper and lower extremities, the sacral region and buttocks, and the shoulders are favored. The face, too, is commonly involved and to a lesser extent the trunk. The lesions are sparse, though the number present varies considerably. The mucous membranes are not involved. The course is chronic over a number of years and cyclical, exacerbating or recurring in the summer. During the active period there are smaller cycles of special activity followed by partial relief. A single lesion takes from ten days to three weeks from onset to subsidence. Itching is intense and brings the patient to the physician for relief. As a result of the distress there may be sleeplessness and nervousness, poor appetite, thinness and anemia.

Etiology

Investigations have not substantiated presumptions that there are food or environmental allergens responsible for the disorder. The subjects, usually children, are mostly of the nervous, tense type and come from the lower half of eco-

nostic classes. A few exceptions to this occur. Nutritional deficiencies have been searched for, but not found. This view was prompted by finding that patients often improve spontaneously when removed from their old environments to a hospital. Food brought from home did not retard such improvement. Some have felt that dust and dirt may be responsible for the malady, but this is not widely accepted. Intoxications and infestations by insects have likewise been blamed. No known cause has been demonstrated with certainty.

Differential Diagnosis

Lichen urticatus is most frequently confused with *scabies*. Both itch intensely, though the latter asserts itself more at night. Scabies is highly contagious and appears in other children and members of the family. It does not involve the face, except in young infants. Scabies affects the finger webs and male genitalia and has the distinctive linear burrows. Lichen urticatus usually has no vesicles and has the characteristic conical, discrete papules.

Prurigo has been confused with lichen urticatus but is much rarer in this country. It, too, affects extensor surfaces and is highly pruritic but is not seasonal in the way that lichen urticatus is. Prurigo develops after some time, causes thickening and lichenification and increase of pigmentation in the skin.

An early case of lichen urticatus often mimics *insect bites*, especially when some of the lesions are wheals. The puncta of wheals from insect bites cannot always be readily distinguished from the excoriated wheals in lichen urticatus. Insect bites are not apt to be as symmetrically disposed as are the lesions of lichen urticatus. Nonetheless, in some cases it is necessary to observe the patient a while before it is possible to distinguish between these two entities.

Eczema is likely to be moist and to produce crusting at times and in chronic states lichenified patches develop. The flexors are involved more than the extensor surfaces. The seasonal variations are not as marked as the cycles of lichen urticatus.

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EXTERNAL AGENTS.—*Colloidal baths* of starch and soda are helpful and appreciated. They are best used before bedtime and are an aid in improving sleep and relieving itching. The water for the bath is drawn as usual for quantity and temperature. For a full size bath, dissolve first one teacup of sodium bicarbonate. No solid, undissolved particles should remain at the bottom of the tub as these irritate. Then two cups of corn-starch or of Linit are mixed thoroughly with hot water in a kettle, and this is poured into the bath. The starch element may be prepared by boiling two cups of oatmeal in a double boiler until thoroughly cooked and then enclosing in a cloth bag which is placed in the bath.

Lotions are better than salves, especially since lichen urticatus is a warm weather disease. Phenol 1 to 2 per cent, menthol 0.5 to 1 per cent or camphor chloral 1 to 2 per cent may be incorporated in calamine lotion to combat pruritus. Still better for this purpose is the inclusion in the lotion of coal tar solution or liquor carbonis detergens in a 3 to 10 per cent strength. The prolonged use of the baths and lotions dry the skin. Some patients apparently are not inconvenienced by this but others complain about it or develop more itching on its account. If the effect of this lotion then becomes too drying, olive oil may be added in equal quantity to the lotion, or glycerin may be incorporated in the lotion in 10 to 20 per cent strength.

A few individuals appreciate *ointments* more than lotions, though the ointment should have some powder in it. Starch and zinc oxide alone or combined to a total of from 10 to 25 per cent may be added to the petrolatum base. With this may be incorporated from 3 to 6 per cent crude coal tar. Fresh applications of lotion or ointment should be preceded by gentle cleansing with mineral or olive oil to prevent the irritation from caking of older applications.

Antipruritic powders may be well borne. A favorite is Anderson's, of which there are several modifications. An example of one of these is camphor 6 per cent in equal parts of zinc oxide, zinc stearate and talcum.

Pyogenic complications should be cared for as indicated under impetigo.

Treatment

The treatment of lichen urticatus has not met with spectacular success. In severe and stubborn cases it is helpful to remove the child temporarily to the hospital until the lesions and itching subside and the child has had a chance to recuperate from the effects of restless sleep. The child's room should be bare of objects that collect dust. The surroundings of the child should be quiet and peaceful, and he should not be exerted or expected to participate in competitive exercises or play. Individual articles of the diet are not known to aggravate lichen urticatus.

INTERNAL MEDICAMENTS.—Internal medication is depended upon in a large measure. A short course of arsenic in the form of *Fowler's solution* may be helpful. The dose is from one to three drops three times a day, given not longer than three weeks. *Quinine*, too, may be given for its tonic effects. *Bromides* are valuable in soothing increased tension and restlessness. The well-known frequency with which eruptions follow their use should be kept in mind and possible complications watched for.

Calcium is of benefit. It should be given in large doses: the lactate in teaspoonful doses twice a day, half an hour before meals. More palatable forms of calcium may be given, such as *Calcilact* in teaspoonful doses two and three times a day. It is more practical to give calcium by mouth at regular intervals in order to get a more even rise of calcium blood level. Injections at longer intervals do not achieve this. Calcium metabolism may also be influenced by the giving of *parathyroid extract*; three to six minims may be given three times a week hypodermically. The combination of calcium by mouth and parathyroid extract is helpful or curative in about 70 per cent of cases. It should be tried for three weeks before being discarded.

Liver extract given by injections is helpful in some cases; 1 to 2 cc. of the one anti-anemic unit to the cubic centimeter may be given every other day.

Vitamin B complex may be tried. Brewer's yeast tablets are a convenient way to administer this, two to ten tablets a day being given.

parently following in its incidence the degree of temperature and humidity. Impetigo is often a complication of some itching dermatosis, where scratching inoculates the pyococci. The most common preceding disorders are the infestations of scabies and pediculosis, especially of the scalp. In every case of impetigo it is necessary to determine whether some cause for itching preceded the impetigo.

Differential Diagnosis

Impetigo of small proportions on the face may be confused with *herpes simplex*. The latter is usually on or near mucocutaneous junctions, has deeper vesicles which do not rupture easily and are grouped. Herpetic lesions may be secondarily infected and become impetiginized and this propagates itself to new sites.

Vesicular eczema may at times be mistaken for impetigo, but is apt to be present a much longer time than is impetigo and is more indurated. It is more symmetrically distributed and usually itches more. The crusts of impetigo are made of elements about fingernail size and more superficial in character. Eczema is apt to produce patches, whereas impetigo elements are irregularly disseminated.

Parasitic sycosis develops nodes and nodules, giving an irregular undulating surface to the beard, especially below the mandibles. *Coccigenic sycosis* has small pustules displayed at the sites of hairs. These elementary lesions may coalesce to form patches that simulate impetigo crusts, but outlying discrete lesions will help in making the diagnosis.

Other disorders to differentiate are *pemphigus vulgaris*, which often imitates impetigo initially, and crust-forming drug eruptions, such as those from bromides.

Treatment

Isolation of victims should be the first procedure. In institutions where epidemics appear and especially in obstetrical wards, strictest measures to accomplish this should be taken early. Attention should be paid to the possibility of spread through common use of mediate objects.

In a few patients with widespread eruptions there may be mild to moderate constitutional changes which require symp-

With some care lichen urticatus can be ameliorated or cleared entirely. In time most subjects are freed of their eruptions, though the physician should not promise cures within definite periods.

IMPETIGO CONTAGIOSA

As the name implies, this is a highly contagious disease due to pyogenic organisms and affects children more often than adults. The exposed parts—face, ears, neck, hands and forearms—are the ones commonly involved, but any part of the skin may be affected. In rare instances it affects the mucous surfaces of parts opening onto the skin. Its first manifestation is a reddish spot which quickly goes on to vesiculation or bullous formation and later still the lesions contain pus. At the latter stage the surrounding skin develops a red areola. The blisters or pustules break easily and discharge a gummy material which dries into crusts. These latter are honey-colored, superficial, thick, and easily removed from their bases, sometimes turned up slightly at their edges. They give the appearance of having been stuck on like bits of clay against a brick wall. The bases below the crusts are moist, red spots that exude a viscid material and are sharply outlined.

Healing of individual lesions takes several days, though it may be longer. The crusts drop off, leaving pinkish sequelae, sometimes with some pigment. This fades out in time. There is no scarring, except rarely with debility or improper treatment. Lesions appear at new and old sites irregularly so that a composite of various stages of evolution may be seen. Besides this, excoriations may be seen in amounts depending upon the degree of itching. This varies from the trivial to moderate, and rarely is severe.

Etiology

The cause of impetigo is cutaneous infection with either staphylococci or streptococci or both. Children are affected more often because of their more intimate contacts while at play, though adults are affected fairly frequently. The barber shop is said to be a common source of infection for the latter. Obstetrical wards and children's institutions may suffer from epidemics. The disease is most prevalent in the summer, ap-

striction. The combination of mercurials for wet dressings, ointment, dusting powder and baths are quite efficient. They should not be preceded or followed by the use of *sulfur* or *iodine* on the skin. *Cinnabar*, a chemical combination of mercury and sulfur, may be used with sulfur. *Colloidal calomel*, 5 to 10 per cent in ointment form, is efficient in eradicating the lesions of impetigo.

Many observers believe that at the present time the use of ammoniated mercury is not attended with as much success as it was formerly. For this reason it becomes doubly necessary to have other agents to substitute for it. *Sulfur* in 2 to 10 per cent salve is an efficient remedy. This is especially helpful in impetiginized scabies. The *dyes* are good, in dispensary practice especially. The best of these is gentian violet in 2 per cent aqueous solution. If it is used for some time, it may irritate, so that a 0.5 to 1 per cent solution may be continued. Other members of this group are methylene blue and brilliant green. The crust should first be removed before applying the dye, such as gentian violet, which dries the secretions as well as inhibits the gram positive cocci.

The use of *silver nitrate solution* as a wet dressing and as a paint causes prompt improvement of the lesions and is curative. For the wet dressings 0.5 per cent aqueous solution reduces the amount of exudate and painting the bases of the lesions with 5 to 10 per cent solution dries them and is followed by rapid epithelization.

Occlusive dressings often are curative. A model for this purpose which has been used a good deal is metaphen 1:500 in collodion. It is applied in thin layers over the lesions in successive layers several times a day. In some cases, however, pus continues to collect beneath and undermines them. In a few cases these occlusive dressings are irritating and have to be discontinued.

Chlorhydroxyquinoline in combination with benzoyl peroxide is an extremely efficient remedy. It is difficult to prepare but a good proprietary ointment that incorporates them is called Quinolar Compound Ointment. It may be applied two to three times a day. As with the use of other agents, quicker action is obtained when the crusts are first removed by preliminary softening with a wet dressing.

tomatic treatment. This applies particularly to infants in whom impetigo is a serious disease and sometimes fatal. The same may be said for the rare case that develops nephritis as a complication from this infection.

It is questionable if in the average case the oral use of the *sulfonamides* is justifiable in a simple, fairly easily cured disorder such as impetigo generally is. In certain debilitated individuals or infants, sulfathiazole should be the sulfonamide given. Some have recommended sulfanilamide as more efficacious than sulfathiazole. This probably depends upon whether streptococci are the dominant organisms in the presenting lesions.

LOCAL MEASURES.—Otherwise impetigo is treated by local measures and in almost all cases this is all that is needed. These all make use of antiseptics for destroying the contagion. The agent universally used, the one that has stood the test of time, is *ammoniated mercury*. This is applied in ointment form, usually in a petrolatum base, in 2 to 10 per cent strength. Before applying the salve, the crusts should be removed by the use of wet dressings. Saturated boric acid solution or a 1:5000 aqueous solution of mercury bichloride applied as wet dressings soften the crusts and they can then be gently brushed off or picked off with forceps. When the crusts are off the ointment is rubbed into the bases, with special attention paid to the undermined edges of epidermis at the margins. Continuous use of the ointment softens any crusts which reform so they may be readily removed. New lesions should be watched for and treated as they form. A word of warning should be given to the patient to expect new lesions to appear for a few days after commencing treatment. Sites near the presenting lesions should be anointed before applying the salve to the actual lesions. This helps to prevent their spread.

If circumstances forbid the use of an ointment during the day, a *calomel powder* in 10 per cent concentration incorporated in equal parts of zinc stearate and talcum may be substituted. In widespread infections, *baths of mercury bichloride* in 1:10,000 strength are useful, though they should not be used more than three or four times in as many days. *Potassium permanganate baths* 1:10,000 are free from this re-

smooth but the surface thickens into a sort of corrugated and folded membrane. This is dry and cracks, exposing a red base through the fissures which run crosswise to the length of the lips in somewhat parallel lines. In time the surface turns to some shade of grayish-brown. The lesions feel dry and may have a burning sensation and induce repeated licking of the surface. At times the lips are tender and with fissuring there may be pain. Subjective symptoms, however, are always mild or trifling. Lymphangitis or enlargement of draining lymph glands do not follow, nor does the infection spread to the neighboring skin or mucous membrane beyond a narrow fringe. Healing occurs, leaving an opalescent surface which then assumes the normal color of the lips. There is no scarring or atrophy.

Etiology

Infection with a species of yeast, the *Monilia albicans*, causes most cases of perlèche. The bacteria present are of different kinds, especially streptococci, which older authors felt caused some or all the cases. In old age or in persons who wear too low dentures so that a fold of skin forms running out from the corners of the mouth, persistent perlèche or perlèche-like lesions may form. In some malnourished persons perlèche-like lesions may form and these changes have been traced to insufficient vitamin B₂ or riboflavin in the diet. Children are the most common subjects for the ordinary variety. There may be epidemics, especially in institutions for children.

Differential Diagnosis

Perlèche needs to be distinguished from *mucous patches* and *split papules of syphilis*. In mucous patches there are erosions and these heal rapidly and shift about. Darkfield examination may help in the diagnosis. In some instances it may be impossible to tell one kind of lesion from the other but observation of the entire individual and serum tests will show that syphilis is present or absent. Yeasts may be present as saprophytes in lesions of the folds due to other causes. Their presence in small numbers does not rule out syphilis. Syphil-

Some feel that the best remedy now is the local use of the *sulfonamides*. These are capable of eradicating the eruption in three to ten days when properly used. The best of this group is *sulfathiazole*, which may be incorporated in various bases. Two that have been recommended are vanishing cream and ordinary surgical lubricating jelly. Probably any simple grease will serve as well. Sulfathiazole should be finely powdered and used in 5 to 10 per cent strengths. After a day's use the crusts blacken and begin to loosen and separate. It is yet too early to say that the sulfonamides constitute the local treatment of choice, but certainly it may be said that they are a powerful addition to weapons against impetigo. In the serious and sometimes grave infections in infants they should be the first to be tried.

Suberythema doses of *ultraviolet light* are valuable in preventing the spread of the disease to other parts. The irradiated areas should be clean and free of grease and medications. The removal of stubborn thickened and large patches of impetigo can be implemented by exposures to quarter erythema doses at five-day intervals for a total of two treatments.

In almost all but young infants, impetigo is fairly easily cured. In them and in debilitated subjects the prognosis at times is bad. If impetigo seems unduly difficult to eradicate, an underlying primary disease such as scabies may have been overlooked or a wrong diagnosis made.

PERLÈCHE

Perlèche belongs to the group of disorders due to yeast infection known as the moniliases. They occur at various sites but always where there is plenty of moisture, as in the body and skin folds. Perlèche is the yeast syndrome which involves the fold at the lip commissures.

The condition usually clings to the fold only but at times may spread towards the midline of the lips. A narrow zone of the adjoining skin and mucous membrane may be involved besides the vermilion border itself. Early there is a whitish, sodden appearance to the epidermis that is sharply defined and that soon looks parboiled. At first the surface is

MISCELLANEOUS SKIN DISEASES

JAMES R. WEBSTER, M.D.*

ACNE VULGARIS

Few if any skin disorders are easier to diagnose than acne vulgaris, but at the same time few will require more patience and perseverance on the part of both physician and patient in their management. It occurs from the ages of eleven or twelve to around thirty but is most widespread and active during the period of adolescence.

Unfortunately there is no specific treatment but, with patience and some understanding of the pathogenesis of the disorder, both the active manifestations and sequelae of the disease can be reduced to a minimum, thereby saving the patient a great deal of mental anguish and embarrassment.

Etiology

Acne, which is present to a greater or less extent in all adolescents, consists primarily of an activation of the sebaceous system. This activation is not completely understood but is a more or less physiological concomitant of the changes in the endocrine balance occurring in adolescence. *Blackheads* form, owing to retention of the sebum in the excretory ducts and hair follicles where it becomes inspissated and mixed with cast-off epithelial cells to form a plug. By pressure this plug may decrease the nutrition and resistance of the perifollicular tissues and infection by the bacteria on the skin and in the ducts occurs. Most of the inflammatory lesions of acne begin in this manner, although some may arise independently of blackheads, since the skin as a whole seems to be lacking in resistance to invasion by surface organisms. It should be

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itic rhagades leave scars, whereas perlèche does not. In *eczema* at the corners of the mouth this is only part of more widespread involvement; patches can be seen elsewhere.

Treatment

As in most instances of yeast infection, one of the requisites is to keep the parts dry. In perlèche it is helpful to gain the cooperation of the child to stop licking the lips. Of all the remedies proposed, *gentian violet* stands first in the treatment of these monilial infections. It may be used in 1 to 2 per cent strengths in aqueous solution or in 25 to 50 per cent alcohol. Applications are made with an applicator to the immediate area twice or three times a day. Following this with the application of *Gram's iodine solution* is still more effective. Ordinarily the infection is speedily brought under control by the use of gentian violet alone, however, tincture of iodine has been much used and is effective. It is safer to dilute it two to four times in alcohol to prevent irritation of the delicate lip tissues.

Other good remedies suggested are 3 to 10 per cent *silver nitrate*, *copper sulfate* solution 2 to 8 per cent; *ammoniated mercury* 1 to 5 per cent, and *yellow oxide of mercury* 3 to 5 per cent in ointment form. Some recommend *Whitfield's ointment* but it should not be used in full strength but rather in one-quarter to one-half strength. Infants and children should be watched for swallowing of applied mercurials. Thick applications are not necessary. Gentian violet does not have this danger.

In subjects with improper dentures these have to be remade so as to raise the bite and iron out the creases radiating from the commissures. The active cooperation of the dentist will speedily clear an otherwise persistent and resistant perlèche.

Riboflavin administration is of no value in the ordinary case of perlèche. In the variety founded on malnutrition, this vitamin is specific and begets spectacular cures.

In all cases care should be taken to prevent spread of the contagion to others by the use of common drinking vessels and other utensils. This is doubly important in institutions for children where isolation will prevent epidemics.

sired *lotio alba* (N.F.) may be used on the face in the morning in addition to the above.

The following *powder* will be found of value for the upper chest and back:

R Powdered camphor	6.00
Precipitated sulfur	10.00
Boric acid	15.00
Powdered starch,	
Powdered talcum	āā q.s. ad 60.00

Blackheads which are not inflamed should be removed periodically with a comedone remover and superficial pustules should be evacuated, but the tissue should not be traumatized.

Internal treatment will depend on the individual case. Any gastro-intestinal derangement should receive attention according to the indications. If the basal metabolic rate is low, *thyroid* should be administered in appropriate dosage. Some authorities recommend its use in practically all instances. Cases in which there is an associated anemia may be benefited by small amounts of *arsenic*.

In addition to the above special measures, or if none of them are indicated, *quinine* is often of great value in those cases with considerable pustular element. It is administered as the bisulfate in doses from 2 to 5 grains three times a day, depending on the patient's age, weight and tolerance to the drug. *Foreign protein therapy* frequently helps those individuals who have persistent deep-seated cystic lesions, but stock vaccines seem as effective as autogenous preparations.

The importance of the *diet* is considerably overestimated by most lay persons and many physicians. It is desirable to avoid iodides, including iodized salt, and bromides, and it should be remembered that bleached wheat flour contains a definite amount of bromide ion. In addition, an excessive amount of chocolate and very rich foods should be avoided, but aside from this a balanced diet is all that is required, and the rigid elimination of sweets seems to be without practical foundation.

Ultraviolet light is of symptomatic benefit but cannot be regarded as curative. *X-rays* properly administered are of great value but it is well to restrict their use to older patients

pointed out that internal *foci of infection* are not of great importance in the pathogenesis of acne. Indirectly they may contribute to the lowering of the resistance of the skin, but in this connection gastro-intestinal derangements, certain dietary indiscretions, demonstrable endocrine disorders and improper local care of the skin are of greater moment.

The disorder occurs on the face, neck and upper trunk. In these regions, on the background of excessive oil and comedones, there are present all types of inflammatory lesions from superficial papules and papulopustules to deep-seated indolent abscesses. The degree of scarring varies with the type of lesions and the management it has received. Some of the lesions may be tender and painful. There is often an associated seborrhea and scaling in the scalp.

Differential Diagnosis

The differential diagnosis should take into account *rosacea*, which occurs at a different age period and is confined to the face, especially the central third; *bromide* and *iodide eruptions*, which are not confined to the acne areas and usually lack the oily background and in which a history of ingestion of the drug may be obtained; and *folliculitis*, which is confined to the bearded region whether it be of bacterial or mycotic origin.

Treatment

In all cases, *soap and water* should be used for cleansing rather than creams, but mild toilet soaps are usually astringent enough, and extremely hot water, steaming the face and the use of complexion brushes should be avoided.

The following *lotion* may be used on the face in general in the evening:

R Sodium baborate	10 00
Zinc oxide	15 00
Powdered starch	15.00
Lime water .	120 00
Rose water	qs ad 240 00

After this has dried an ointment containing 2 to 3 per cent *salicylic acid* and 3 to 5 per cent *precipitated sulfur* should be applied to the lesions. If more intensive treatment is de-

transient, being precipitated by the taking of food or drink, exposure to the elements or excitement. Gradually it becomes permanent and eventually small telangiectases appear especially on the nose, cheeks and chin. After a variable length of time the face becomes oily and there are comedones and acneform lesions of all types chiefly on the central portion of the face. When these are developed the disorder is in the *second stage*. In a few instances, after months or years, the *third stage* supervenes with an enlargement of the tip and alae of the nose due to hypertrophy of the *sebaceous* glands. In a well developed case of *rhinophyma* the nose is red, bulbous, rough and nodular, with dilated duct orifices filled with sebum and many telangiectases; in short, "beer drinker's nose."

Etiology

Many factors may be concerned in causing this clinical picture. In women, gynecologic disorders and the menopause are sometimes involved. In the dietary, the taking of stimulants such as alcohol, tea and coffee in excess is certainly an aggravation. Digestive disorders are important in many cases and two phases of this warrant particular mention: first, low gastric acidity, and second, improper intestinal fat digestion. Foci of infection apparently are to be implicated in some instances.

Differential Diagnosis

Lupus miliaris disseminatus faciei and the so-called *rosacea-like tuberculid* may sometimes be confused with rosacea, but in both of these the disorder is not limited to the central third of the face, the oily background with comedones is usually lacking, and diascopic pressure will reveal the apple-jelly brown of the tuberculodermas.

Treatment

Obviously no treatment of acne rosacea is sound without a thorough check of endocrine and gastro-intestinal functions and search for foci of infection. Any indication presented by such examination should be followed. Even in the absence of definite findings, improvement has been frequently

because of the danger of recurrence of the acne in individuals under sixteen or eighteen years of age. X-rays should never be used to the exclusion of other measures nor should they be used in frankly pustular cases.

By the judicious use of some or all of these measures, together with encouragement of the patient, much can be accomplished, but the doctor and patient should both realize that specific treatment is not available, that improvement will be slow and subject to periodic setbacks, and that the chief aims of treatment are to keep the activity at a minimum and avoid scarring as much as possible until management and/or the arrival of adult age shall bring the disorder under control.

Adolescent individuals with acne, especially girls, are much embarrassed by "bad complexions" and frequently this embarrassment may have a rather pronounced effect on the personality. In such cases *sympathetic understanding* on the part of the physician is most necessary. Too often the situation is made worse by the fact that the doctor pays very little attention to the patient's frame of mind, as a result of which confidence on the patient's part wanes, the patient becomes much discouraged and fails to carry out the treatment or seeks advice elsewhere. Encouragement is justifiable and necessary but the patient should realize that the eradication of the disorder is something that requires much time and perseverance and that flare-ups will invariably occur from time to time for a considerable period. If these facts are made clear early in the association of doctor and patient the results of treatment will be much better, and a patient who might otherwise develop a distinctly introverted personality will be able to maintain a proper relationship with his or her associates until the skin condition has been improved.

ACNE ROSACEA

Acne rosacea (also called simply rosacea) is seen chiefly after forty but occasionally as early as the third decade of life. It occurs in three stages, although the dividing line between them is not sharp and, today, development of the third stage or rhinophyma is very rare. The *first stage* is one of erythema affecting the central third of the face, at first

tion with its characteristic arrangement of lesions, and clears spontaneously in a few weeks. *Psoriasis* in the scalp alone may offer a difficult differentiation but is more patchy and itches less. *Sensitization dermatitis* (eczema) shows more diffuse involvement of affected areas and fails to show well defined lesions. *Ringworm* shows a great tendency for central involution on the glabrous skin. and in both skin and scalp lesions the causative organism is easily demonstrated.

Etiology

Seborrheic dermatitis is an infectious process, the organisms gaining access to the skin from the outside. Moisture, friction and uncleanness may be predisposing causes, and any debilitating constitutional disease may cut down the resistance of the skin to allow the process to begin. Many organisms have been isolated and it is probable that not one but several may produce the picture. Secondary infection with pyrogenic cocci is not infrequent. There is no definite evidence of transmissibility of the disorder and this favors the lessened resistance as an important predisposing cause.

Treatment

When the disorder is acute, soothing and mildly antiseptic measures should be employed. At such times soaks with warm 1:2000 *potassium permanganate solution* are helpful on skin lesions along with *calamine lotion* if they are moist and *Lassar's paste* with or without 2 per cent ichthyol if they are dry. In the scalp, *boric acid* soaks might be used and 1 to 2 per cent *salicylic acid* in petrolatum or oil used between soakings. Intravenous injections of *sodium* or *calcium thio-sulfate* may be of great aid at this time. Soap and water should be avoided.

In the chronic phase of the disorder stronger preparations are permissible. *Sulfur*, *ammoniated mercury* and *tar* preparations are all recommended. although sulfur and mercurials should not be used concomitantly in any patient. In the scalp an ointment of 5 per cent sulfur in equal parts of cold cream and vaseline could be used once a week, allowed to remain on overnight and the scalp washed next morning. Two or

noted following the use of small amounts of *dilute hydrochloric acid*, *bile preparations* or *intestinal antiseptics* by mouth. In very active cases *foreign protein therapy* may be of value. Stimulants, highly seasoned foods, extremes of temperature and excess of fats should be avoided.

The local treatment is essentially the same as that for *acne vulgaris*. When the inflammatory component is under control, the persistent erythema can be greatly improved with destruction of superficial telangiectases by *electrolysis*. Because of the erythema, x-rays should be used with great caution if at all, and ultraviolet light is often an aggravation. When inflammatory lesions are no longer present, any existing rhinophyma may be improved by *surgery*, repeated light *electrodesiccation* or the application of *trichloroacetic acid*. Even though the surface epithelium is largely destroyed by these measures, re-epithelialization originating from the duct passages takes place promptly.

SEBORRHEIC DERMATITIS

Seborrheic dermatitis originates in the pilosebaceous system and therefore is most marked on the scalp, about the face and ears, and in the axillary, inguinal, sternal and inter-scapular regions. It is chronic but has periods of exacerbation.

Symptoms

The most common manifestation is a persistent, oily, adherent scaling of the scalp with itching, which leads, after long periods in men particularly, to alopecia. Seborrheic dermatitis occurs on the skin as well defined, reddened patches with a yellowish greasy scale and considerable itching. The lesions spread peripherally but there is no tendency to central involution. At times the lesions become acutely inflamed and there is much exudation of a yellowish serous fluid which, in the scalp, mats down the hair, and wide extension may occur.

Differential Diagnosis

The diagnosis is usually fairly evident, taking into account the nature and distribution of the lesions. *Pityriasis rosea* commonly does not itch, appears suddenly in wide distribu-

tion with its characteristic arrangement of lesions, and clears spontaneously in a few weeks. *Psoriasis* in the scalp alone may offer a difficult differentiation but is more patchy and itches less. *Sensitization dermatitis* (eczema) shows more diffuse involvement of affected areas and fails to show well defined lesions. *Ringworm* shows a great tendency for central involution on the glabrous skin, and in both skin and scalp lesions the causative organism is easily demonstrated.

Etiology

Seborrheic dermatitis is an infectious process, the organisms gaining access to the skin from the outside. Moisture, friction and uncleanness may be predisposing causes, and any debilitating constitutional disease may cut down the resistance of the skin to allow the process to begin. Many organisms have been isolated and it is probable that not one but several may produce the picture. Secondary infection with pyrogenic cocci is not infrequent. There is no definite evidence of transmissibility of the disorder and this favors the lessened resistance as an important predisposing cause.

Treatment

When the disorder is acute, soothing and mildly antiseptic measures should be employed. At such times soaks with warm 1:2000 *potassium permanganate solution* are helpful on skin lesions along with *calamine lotion* if they are moist and *Lassar's paste* with or without 2 per cent *ichthyol* if they are dry. In the scalp, *boric acid* soaks might be used and 1 to 2 per cent *salicylic acid* in petrolatum or oil used between soakings. Intravenous injections of *sodium* or *calcium thio-sulfate* may be of great aid at this time. Soap and water should be avoided.

In the chronic phase of the disorder stronger preparations are permissible. *Sulfur*, *anhydrous mercury* and *tar* preparations are all recommended, although sulfur and mercurials should not be used concomitantly in any patient. In the scalp an ointment of 5 per cent sulfur in equal parts of cold cream and vaseline could be used once a week, allowed to remain on overnight and the scalp washed next morning. Two or

three times a week the following lotion could be applied to the scalp using a medicine dropper:

R. Euresol	8.00
Spts. odorati	30.00
Alcohol, 50 per cent	qs. ad 240.00

Five per cent crude coal tar in chloroform makes an effective scalp application.

On the skin at this stage 3 to 5 per cent sulfur, 5 per cent crude coal tar, or 3 to 5 per cent ammoniated mercury in ointment form are all of value. X-ray properly employed on the glabrous skin will often be helpful.

Arsenic in small doses will be found beneficial in the chronic stages of the disorder but its administration should be carefully watched. Cultural examination probably should be made in all cases. If streptococci are found, the local treatment should be largely with *mercurials*, and *sulfanilamide* might be given orally.

PITYRIASIS ROSEA

Pityriasis rosea is a self-limited disorder with a characteristic course. Commonly one lesion appears on the trunk as a coin-sized, round or oval, superficial, very slightly indurated reddish plaque, the surface of which is covered with a fine adherent scale, often not perceptible unless subjected to friction. There is usually no sensation and if it is not visible to the patient the lesion may be overlooked and this probably accounts for the fact that many patients do not give a history of this "herald spot."

A few days to a week later, a more or less generalized eruption appears. It is rare for the face and scalp to be involved, and unusual for the eruption to spread distally on the extremities beyond the elbows or knees. The lesions are similar to the herald spot, though smaller and more generally oval. They are for the most part arranged with their long axes parallel to the lines of cleavage of the skin. New lesions develop for a week or two, then the picture remains stationary for ten to fourteen days after which spontaneous involution begins so that recovery is usually complete in from six to

eight weeks after the onset. Itching is only slight unless the disorder is particularly widespread and active.

Etiology

The cause of pityriasis rosea is not known. No statistics are available but it seems probable that a large percentage of individuals have the disease once and, for one reason or another, at a time when their resistance might be considered to be low. This fact, coupled with the self-limited character of the disorder and the fact that a second attack in any one person is extremely rare, suggests a similarity to the exanthemata, but no organism has been generally accepted as an etiologic factor.

Differential Diagnosis

The self-limitation and the nature, distribution and arrangements of the lesions serve to differentiate pityriasis rosea from *psoriasis* and *seborrheic dermatitis*. Widespread ring-worm of the glabrous skin is more itchy, there is central involution of the lesions and the causative organism may be demonstrated. *Secondary syphilis* should always be kept in mind but in syphilis there are mucous membrane lesions as well as a generalized adenopathy and occasional constitutional symptoms in addition to the skin manifestations, and the serology, at this stage, is always positive.

Treatment

Since the disorder is self-limited, treatment is not essential unless itching is marked, in which case soothing preparations such as *calamine lotion* or 1 to 2 per cent *salicylic acid ointment* may be used. Two or three generalized mild erythema exposures to *ultraviolet light* will shorten the course.

HERPES SIMPLEX

Herpes simplex occurs most commonly about the mouth, face and external genitalia, but may be seen anywhere on the cutaneous surface. A stinging or burning sensation is felt, followed in a few hours by a fairly well defined erythematous spot in which several pinhead-sized, deep-seated vesicles soon

appear. Commonly, the vesicle fluid becomes turbid and the vesicle desiccates without rupture in a few days leading to some scaling which, with the redness, disappears gradually, the disorder running a self-limited course of five to ten days. In other cases, however, with or without secondary infection, there is more inflammatory reaction with exudation and crusting, possible enlargement of regional glands and a somewhat longer course. Recurrences are common and usually in the same spot, and it is this phenomenon which causes patients to seek advice.

Differential Diagnosis

Except in very marked cases, differentiation from *herpes zoster* is not difficult, taking into account the history of recurrence, absence of severe pain and marked regional adenyopathy, the singleness of the lesion and absence of radicular distribution. A very inflammatory lesion might at first be confused with *impetigo* but a few days' observation will clear up the confusion.

Etiology

Besides the association with colds and general infectious diseases, herpes simplex is seen following exposure to sun and wind, after trauma and in gastro-intestinal upsets, or without connection with any other demonstrable disorder. These conditions apparently act as precipitating causes by decreasing the resistance, for it has been generally recognized that the cause of herpes simplex is a *filtrable virus* apparently entering the system through the respiratory passages. The ultimate localization of the virus seems to be about the sensory nerve endings, resulting in the production of the lesion. Recurrence in the same area is explained by the development of a *locus minoris resistentiae*, a new infection or reactivation of the virus which has remained dormant in situ since a previous attack.

Treatment

In the ordinary case on the skin *calamine lotion* does well for the first few days. If there is much reaction this can be combined with *boric acid* soaks. After the lesion has desic-

cated a soothing ointment such as unguentum zinci oxidi (U.S.P.) may be used. If there is secondary infection the treatment suggested for impetigo may be used with benefit. More of a problem is the prevention of recurrences. Several procedures have been advocated, all of which apparently have been successful in some instances and failed in others.

A series of two to four fractional exposures of the region involved to x-rays at ten-day intervals is justifiable and often apparently successful. Repeated *vaccination* with cowpox virus as used for smallpox may be tried and, finally, vaccination with the patient's own blister fluid at the onset when the vesicles are still clear has in some instances appeared to terminate a series.

HERPES ZOSTER

In herpes zoster, the eruption follows the course of some sensory nerve. Pain, often intense, is usually associated with the skin manifestations; it not infrequently begins a few days before the appearance of the eruption and, particularly in elderly and cachectic individuals, persists after the skin lesions have disappeared.

The eruption is composed of thick-roofed vesicles on inflammatory bases and the groups are arranged essentially along the distribution of a sensory nerve. Zoster apparently is the result of a sensory ganglionitis and the eruption will appear in the distribution of fibers from the involved ganglion. Therefore, in cases of involvement of ganglia in the brachial and lumbosacral plexuses, the distribution may not be exactly limited to the course of one peripheral nerve. If the gasserian ganglion is involved, the distribution of one or more branches of the fifth cranial nerve will be involved, consequently lesions may be seen on the cornea, in the mouth, in the nose or in the ear canal, as well as on the skin. With very few exceptions the disorder is unilateral and this is often of diagnostic importance. In a few cases a typical zoster is seen accompanied by a scattered generalized eruption, the lesions of which are very similar to those of chickenpox.

The vesicles themselves vary in different cases from small

appear. Commonly, the vesicle fluid becomes turbid and the vesicle desiccates without rupture in a few days leading to some scaling which, with the redness, disappears gradually, the disorder running a self-limited course of five to ten days. In other cases, however, with or without secondary infection, there is more inflammatory reaction with exudation and crusting, possible enlargement of regional glands and a somewhat longer course. Recurrences are common and usually in the same spot, and it is this phenomenon which causes patients to seek advice.

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Treatment

In the ordinary case on the skin *calamine lotion* does well for the first few days. If there is much reaction this can be combined with *boric acid* soaks. After the lesion has desic-

Later 10 per cent *naftalan* or 2 per cent *ichthyol* in Lassar's paste will be agreeable.

When the *ophthalmic division of the trigeminal nerve* is involved there is usually marked swelling of the eyelids, often closing them, and the eye itself is inflamed, painful and vesicles may be present on the cornea. In such cases the eye should receive periodic gentle soaking and irrigation with warm boric acid solution, after each application of which 5 per cent argyrol solution might be instilled or a small amount of 1:3000 bichloride of mercury ointment introduced. The eye should be put at rest between treatments and covered with a patch. In the *ear* 5 per cent phenol in glycerin or 1 to 2 per cent salicylic acid in 50 per cent alcohol is helpful.

Salicylates should be given freely for the pain and the judicious use of *codeine* is permissible if necessary, although care must be taken to guard against addiction. Subcutaneous injections of *pituirin* have been advocated, as have also filtered *x-rays* over the involved ganglion. The latter apparently is quite helpful in some cases but has the disadvantage occasionally of causing marked temporary exacerbation. Intravenous injections of *sodium iodide* in 1- to 2-Gm. doses every other day, if not contraindicated, has proved very effective in many cases for diminishing pain and hastening involution of the process.

Recently there have been many favorable experiences with the use of vitamin B and especially *thiamine chloride* by mouth and by injection, and further use of such therapy is distinctly warranted.

PSORIASIS

This rather common disorder, as a rule quite easily recognized, has up to the present defied investigators both as to cause and the obtaining of permanent relief.

Symptoms

The sites of predilection are the extensor surfaces of the extremities about the elbows and knees, and the scalp, but the disease may occur anywhere on the body surface. The elementary lesion is a flat-topped, bright red papule with

abortive ones to hemorrhagic lesions, and occasionally there is necrosis with resultant scarring, a fact which is of considerable importance in the case of ophthalmic zoster involving the cornea.

Diagnosis

The diagnosis is usually simple, taking into account the characteristics described. An extensive and inflammatory *herpes simplex* may cause some difficulty. The points of distinction have been mentioned in connection with that disorder.

Etiology

One attack of herpes apparently confers immunity. The disorder occurs chiefly in adults but has been seen in children. It has been generally accepted that zoster is caused by a *filtrable virus* localized in a sensory ganglion. The virus is apparently similar to but not identical with that causing herpes simplex and is certainly similar to the varicella virus. Some investigators believe in its identity with the latter virus but the evidence is not absolutely conclusive and this point is still much debated.

Treatment

Herpes zoster is a self-limited disease but requires treatment, first, because of the intense pain often encountered, which sometimes persists, and second, because of the possibility of scarring, especially important on the cornea where it may interfere with vision.

In the early stages, local astringent and protective treatment is indicated. There is often an associated hyperesthesia, and friction and pressure by clothing may be very annoying. The following *lotion*, covered by a protective dressing when possible, will be helpful:

R Phenol	2.40
Glycerin	8.00
Sodium biborate	10.00
Zinc oxide	15.00
Powdered starch	15.00
Lime water	120.00
Rose water	q.s. ad 240.00

currence in two or more generations in the same family have been noted, but this is not common. It seems, however, that whatever the precipitating cause, there must be some inherent potentiality in the individual for the development of psoriasis.

Treatment

EXTERNAL MEASURES.—Because the simpler measures are quite often successful it is always desirable to use them first, and nothing but the simpler measures should be used in acute cases. On the glabrous skin an ointment of 2 per cent *salicylic acid* and 3 to 5 per cent *ammoniated mercury* is of great value, unless the patient is sensitive to the mercurials; in many cases this ointment will be all that is necessary. If it proves ineffective, tar may be used. The combination of 1 to 3 per cent *crude coal tar ointment* with generalized *ultraviolet radiations*, productive of first degree erythema, at short intervals is often effective. In widespread exudative cases 10 per cent *naftalan* in Lassar's paste may be extremely helpful.

Chrysarobin is valuable in stubborn cases of a few lesions on the covered portions of the body, but it must be used with caution and exact directions to the patient are necessary. It is used in 3 to 5 per cent strength in an ointment or in traumaticin, and is applied at night, restricting the application exactly to the involved areas. After a few days a reaction will be noted in the form of redness of the normal skin at the periphery of the lesions, often associated with itching. At such time the use of *chrysarobin* should be stopped, since failure to do so will result in marked reaction and possible severe dermatitis. When the reaction subsides the drug may be resumed as before if the lesions have not cleared, but often the production of the mild reaction will result in the clearing of many of the lesions. Because of its staining of the skin and hair, *chrysarobin* should not be used on exposed portions of the body and, if the hands are used for the application, precautions should be taken that none of the preparation be transferred to the region of the eyes.

In the scalp 3 per cent *salicylic acid* and 5 to 10 per cent *ammoniated mercury in petrolatum* may be used once or

precipitous sides, covered with an imbricated, silvery white scale, thickest in the center of the lesion. With moderate curettage the scales may be removed, revealing pin-point sized bleeding points which represent exposed papillae of the corium. By enlargement and coalescence of the papules, various sized plaques and gyrate forms may be produced. As a rule, there is little or no itching.

In most cases, relatively few lesions are present but they last for months at a time, particularly in the winter. The disorder is apt to clear spontaneously in the summer only to return again the following fall or winter. At times there will be an acute onset, with numerous small lesions appearing suddenly in wide distribution and with rapid extension. When psoriasis is in an active phase, new lesions may be caused by moderate trauma like scratches and pin pricks on normal skin.

The lesions in the *scalp* are essentially the same as those on the glabrous skin, although the underlying red color is usually not as apparent. They may lead to temporary thinning of the hair but not to any permanent alopecia. The *fingernails* are often involved in the form of pitting of the nail substance and separation of the distal portions of the nails from their beds, with subungual hyperkeratosis. In rare instances, particularly on the palms and soles, pinhead to small-pea sized pustules occur in the areas of psoriasis.

The disease is very persistent. It clears either spontaneously or as a result of treatment from time to time, but recurrence is to be expected sooner or later, so that once established it should be expected to last over an indefinite period of years. The general health is not affected but an association of arthritis and psoriasis has occasionally been observed.

Etiology

The cause of the disease is unknown. By many it is believed to be a result of disordered protein or fat metabolism, but conclusive evidence is lacking. Other investigators see a connection with the autonomic nervous system, and still others would regard it as an infectious process either local or resulting from a focus in the body. The disorder is much less common in children than in adults. Many instances of its oc-

much associated inflammatory change of the underlying skin. needs no further description.

Flat Wart

The flat wart of childhood (*verruca plana juvenilis*) occurs as a pinhead-sized to slightly larger, round, flat-topped papule of the same general color as the balance of the skin but with an occasional slightly yellow tinge and with very little change of the surface. Flat warts are seen chiefly on the face and dorsa of the hands in children and are often very numerous. They rarely occur in adults.

Plantar Wart

The plantar wart is entirely analogous to *verruca vulgaris*, but occurring as it does on a weight-bearing surface it does not project above the surface of the skin but rather lies within it and becomes covered with a heavy callus. The lesions are, as a rule, extremely tender and painful and a tender callus on the sole of the foot should always suggest the possibility of an underlying plantar wart. Trimming the callus will reveal the papillomatous tissue underneath, which bleeds easily when cut into.

Verruca Acuminata

Verruca acuminata (*condyloma acuminatum*), often somewhat improperly called "venereal wart," occurs in the genital area or in any region in which there is apposition of tissues and therefore heat, mechanical irritation and retention of perspiration. The individual wart itself is a soft papilloma with a constricted base and an enlarged distal portion with serrated edges (cock's-comb appearance). These lesions are often found crowded together into irregular masses, so that a fungating tumor may be produced. Often there is secondary infection and the group of warts may become covered with dirty, foul-smelling secretions.

Seborrheic Wart

The so-called seborrheic wart occurs in elderly people about the face, head and trunk. Originally they appear much as the flat warts of childhood but become larger, irregular

twice a week with frequent shampooing. Local medicinal treatment of the nails is unsatisfactory.

INTERNAL TREATMENT.—In the internal treatment of psoriasis, *arsenic* holds first rank, but its use should be restricted to the disease in its chronic localized phase, for if it is used in an acute spreading case a generalized exfoliative dermatitis may result. It may be given in the form of Fowler's solution or as arsenic trioxide in the Asiatic pill. The dose will depend, of course, on the patient's age, weight and tolerance to the drug. The patient should never be allowed to take arsenic over a long period of time without the supervision of a physician, since great harm may result.

Salicin in the doses of 5 to 10 grains three times a day before meals, in capsule form, is often of service, particularly in acute cases, as are also intramuscular injections of the patient's own *blood* at five- to seven-day intervals.

Various *diets* have been recommended but their value is at present questionable. Further investigative work along the lines of fat metabolism is warranted, and certainly an individual with psoriasis should not eat an excess of fats.

OTHER MEASURES.—Often a change to a *warm dry climate* will produce marked improvement.

X-ray therapy in small doses is very valuable in clearing up the lesions of psoriasis and is the only effective local measure for the treatment of the nails but, as always in the case of a recurrent disorder, it should be used sparingly and with great caution.

By some one or a combination of the above suggested measures it is usually possible to clear up a case of psoriasis, but it should be repeated and emphasized that until more is known about the etiology we cannot do other than expect recurrence.

VERRUCAE

Verruca Vulgaris

Warts occur on the human skin in several forms. The most frequently occurring type is the so-called verruca vulgaris, probably most common on the hands but seen at times in other locations including the scalp and mucous membranes. The familiar keratotic, dome-shaped lesion, usually without

the warts are not angular, their surface is not shiny and the color is not violaceous. The *plantar wart* may be taken for a painful callus with underlying cornlike keratosis due to pressure, but trimming will reveal the soft papilloma which bleeds easily rather than a hard translucent keratotic core under the callus. If a closely placed group of *condylomata acuminata* has been flattened by pressure it might be mistaken for a condyloma latum of syphilis, but with a blunt instrument the group can be separated so that the individual lesions are seen. A period of observation would clear up any doubt as to whether lesions on the region of apposition were *verruca acuminata* or *pemphigus vegetans*.

The *seborrhoeic wart* may simulate senile keratosis and differentiation is important because the latter has distinct malignant potentialities while the wart has little or no tendency in this direction. In contrast to the wart, the keratosis is gray to black in color rather than some shade of brown, it is a hard, keratotic plate rather than a relatively granular, friable mass, and when forcibly removed it comes off in one piece showing horny projections on its undersurface which had extended into underlying follicle mouths.

Local Treatment

The treatment of warts can be a distinct problem. They occasionally respond to the simplest measures some of which seem to have no rational basis, a fact which has been explained by some investigators as due to suggestion; and on the other hand, they will at times resist the most energetic treatment. In all varieties some form of destructive therapy would seem to offer the best hope of success but especially in the case of *verruca plana juvenilis* this is not always practical because of the danger of scarring.

COMMON AND SEBORRHOIC WARTS.—For the common wart and the seborrhoeic type, softening with *salicylic acid* in 5 per cent strength for a week or so, followed by applications of *solid carbon dioxide* offers quite uniform results without much danger of scarring if the refrigeration is well localized to the lesion itself. If this fails, electrocoagulation may be used.

in outline and the surface becomes granular, usually friable, and varies from light to dark brown or almost black in color.

Warts, particularly the acuminate variety, are auto-inoculable and, if a patient has one lesion, others are likely to appear from time to time. Their course is extremely unpredictable and they may persist for years without change and then either suddenly begin to grow and multiply or equally suddenly disappear.

Etiology

A filtrable virus is apparently the cause of all types of warts except the seborrheic variety and may also be important in the latter, but conclusive evidence is lacking. Apparently the same virus is responsible for all varieties and the difference in form is due to variation in soil rather than seed. In the ordinary case, growth of the virus produces the common wart, but if the delicate skin on the face and dorsa of the hands in children is attacked the flat wart is the result; on the plantar surface of the feet, with heavy stratum corneum and weight bearing, a different type eventuates; and if the virus is implanted in intertriginous regions the macerated condyloma acuminatum makes its appearance. It was originally noted that verrucae acuminatae were associated with gonorrhea and therefore they were named "venereal warts," but they occur just as frequently in people without gonorrhea; the only connection with gonorrhea would be that a discharge might macerate and irritate the skin in the vicinity and thus predispose to the development of warts and modify their picture if present. In the case of the seborrheic wart, opinion is divided as to whether this also is caused by the virus or whether it is a benign manifestation of senile change of the skin. Trauma and maceration of the skin may, of course, be of importance as predisposing causes in all types of warts.

Diagnosis

The common wart offers no difficulty in diagnosis. *Verruca plana juvenilis* at first glance might seem to simulate the lesions of lichen planus but the location is usually different,

GYNECOLOGIC OFFICE PROCEDURES

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TODAY we shall discuss some of the methods of diagnosis and of treatment which may be carried out in the physician's office. Completion of some of the treatments, of course, extends to the home or to the hospital, but they may be initiated in the office. There are many ways in which the art and science of medicine may be applied to achieve the desired ends, and they result from the various viewpoints of the individual physicians. From the standpoint of the urologist, for instance, it has been said that all men either have gonorrhea, have had gonorrhea, or are going to get gonorrhea. Of course, this view is too exaggerated to be taken literally, but the same optimistic delusion may apply to the young and hopeful obstetrician in regard to the fecundity of his women patients. A bit of careful reflection would remind him that not infrequently sterile matings occur even in apparently normal and healthy couples. However, the investigation of the reasons for these frustrated efforts represents an interesting branch of our specialty.

WHAT IS AN ADEQUATE GYNECOLOGIC EXAMINATION?

Physicians are now trained and educated to make thorough and complete examinations of the human machine whenever called upon for some failure of bodily performance or some vague knock in the mechanism. But consider, if you will, how different the approach of individual physicians is to their patients. On the one hand, we see the man who makes a direct diagnosis without a differential diagnosis—a great timesaver, but a hit-or-miss method—who, after a glance at

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FLAT WARTS OF CHILDHOOD.—*Verruca plana juvenilis* will often respond to the application nightly to the individual lesions of *liquor calcis sulfuratae* (N.F.) (Vleminckx's solution). After a time a moderate reaction is set up which often results in disappearance of the lesions.

PLANTAR WARTS.—If technically feasible, *x-ray* or *radium therapy* is probably the treatment of choice for plantar warts. If there are only a few lesions on the soles, the normal skin of the foot may be shielded and from two to three erythema doses of radiation applied to the lesions after any overlying callus has been trimmed as much as possible. This dosage could be repeated in ten to fourteen days if necessary, but if two treatments have not sufficed it probably would be better not to use further radiation. If radiation is not available or technically not practicable because of the number of lesions present, the calluses may be periodically trimmed and *trichloroacetic acid* applied to the papillomatous growths. Perseverance in this routine will usually be rewarded with success.

CONDYLOMA ACUMINATA.—In the care of condyloma acuminata any existing secondary infection should first be attended to by soaking with 1:1500 *potassium permanganate solution* or by some similar measure, after which refrigeration with *solid carbon dioxide* or *electrodesiccation* may be used.

Systemic Treatment

Various types of systemic treatment have been used with varying degrees of success by different investigators. *Arsenic* taken by mouth or by injection has been helpful at times. The intramuscular injection of *bismuth* as in the treatment of syphilis has been advocated, as has also injection of aqueous bismuth preparations into and under the base of common warts. A few attempts at *immune treatment* of warts have been made, using filtrates from ground-up lesions, but their results have, to date, been equivocal.

tor. In the practice of gynecology, while it is highly important to obtain a good history, it is usually unnecessary to go into such detail as to whether every ancestor of the patient suffered from fits, ingrown toenails, or wore glasses. One must only obtain sufficient information from the patient, by means of certain leading questions, to supplement that which the patient volunteers. Complete blood studies and other laboratory data may not be needed in every gynecologic disturbance, but there are certain examinations which are essential for a correct diagnosis. The physician must decide which of these tests should be made, after considering carefully the history and coordinating data so obtained with his findings on examination. Furthermore, he should withhold his diagnosis until he has all the information yielded by these significant and often decisive tests.

I shall not attempt to cover all of the details of a thorough gynecologic examination, or to discuss all the disturbances which might be treated in the doctor's office. But I do wish to touch upon those points which I feel are essential for the intelligent management of gynecologic cases.

THE HISTORY

First of all, in the gynecologic history, it should be a matter of routine to record the usual information which pertains to the *menstrual cycle* as well as the date of the last menstrual period. *Past obstetrical experience* is important. The occurrence of any *vaginal discharge* and its description should be recorded with special accompanying symptoms, such as itching or burning and, often coupled with this, frequent or painful urination. These data may give an immediate clue in cases of certain disturbances.

THE PHYSICAL EXAMINATION

Abdominal Palpation

In the course of the physical examination, palpation of the lower abdomen should always be made before examining the genitalia, for at times a swelling or a mass thus discovered may prove to be a key finding. However, before making an abdominal examination, it is both advisable and politic to

the tongue, a feel of the pulse, writes out a prescription and collects in cash. In striking contrast is the practice of some prominent clinics which make an exhaustive inventory of history and physical findings an ironclad routine, irrespective of the gravity or nature of the patient's ailment. Some individual physicians have found it profitable to imitate the famous clinics in this practice and likewise insist upon complete inventories before even seeing their patients. In the practice of one such physician, an ophthalmologist who has since passed on, the following incident actually occurred:

A gentleman from out of town, while visiting in the "Windy City," got a cinder in his eye. Being unacquainted with any of the physicians in town, he stepped to a telephone and called his own doctor at home for advice as to whom he should consult. He was given the name of Dr.—. He hastened to the doctor's office, and after registering and furnishing the usual data, was placed in a room where a nurse proceeded to take a detailed history. All of his attempts to tell his own story were unavailing. Blood counts, urinalysis and blood pressure, weight, pulse rate and temperature were duly noted. By this time the man was very impatient—tears were flowing down one cheek—and he pleaded to see the doctor immediately. He was informed that he would have to wait until all was prepared for a total evaluation. When led to a dark room where refraction and other tests were to be made by an assistant, the man fled in desperation. He stopped in the corner drug store and asked a clerk whether he could see anything in his eye. The clerk deftly removed the offending cinder and sold him a simple eye wash; complete relief followed. You see, the home physician whom the patient had called, immediately called Dr.—'s office in Chicago and announced the coming of the patient, a prominent citizen of his city, and asked that every courtesy be extended to him. But he neglected to state the nature of man's complaint! Dr.— learned of the episode and told it on himself at a medical banquet.

There is, in the manner of examining patients, a *practical middle ground*. Whether you are a general practitioner or a qualified specialist in any of the various fields of medicine, it is well to bear in mind that the most important thing to the patient is the *complaint* which brings that patient to the doc-

it hardly requires mentioning, but I am led to understand that, in some communities, gloves or even finger cots are omitted. By way of caution, let me remind you that some thirty years ago it was said that 5 per cent of all the then practicing gynecologists had syphilis, with chancre of the finger, which they acquired because of failure to observe this precaution. Not only is there still a danger of syphilitic infection, but it is extremely unesthetic to examine women with gonorrhea or other conditions associated with foul discharges—such as trichomonas vaginitis, yeast infections, ulcerating fibroids and cancer—without the self-protection afforded by rubber gloves.

Bimanual Examination

Before making a bimanual examination, it has been my un-failing practice to have the patient empty the bladder, not only for the purpose of obtaining a fresh specimen of urine for examination, but also because a full or partially full bladder may entirely obscure the real pelvic disease. On separating the labia, first examine the external urethral orifice (Fig. 21). Common lesions observed here are caruncle, skenitis, prolapse of the urethra and, sometimes, marked dilatation of the urethra. Bartholin's ducts are visible only when they are inflamed. Reddening at the orifices of Bartholin's and Skene's ducts usually indicates that the patient has or has had gonorrhea. Urethral smears, and additional smears from the secretion of Bartholin's duct and from the cervix, should always be taken in such cases. When such smears are to be taken, no lubricating substances should be used on the examining fingers until after the smears have been procured. Milking of the urethra may be necessary in some cases before a discharge from the urethra or from Skene's ducts becomes visible.

Bimanual palpation should be made with *gentleness* and *great care*. Rough and clumsy efforts cause the patient to resist and may lead to faulty interpretation. In addition to determining the size, shape, position and consistency of the uterus and adnexae, one should also feel for cervical abnormalities and scars; and, before completing the examination, let me advise you to turn the fingers so that they face pos-

wash your hands in the presence of the patient, thereby indicating to her that her physician is both clean and careful. The palpation of a tumor mass in the lower abdomen immediately suggests the presence of one of the three most obvious conditions in women: pregnancy, fibroids, or ovarian cysts. But the full bladder must not be overlooked! I have discovered the full bladder to be the sole cause of a "painful abdominal tumor" which was referred to me for surgical removal, but which was removed by catheter! I recall seeing a patient a few years ago who had visited a general practitioner because of uterine bleeding. He diagnosed a cervical polyp which could be seen through the speculum, but he completely missed a fibroid the size of a grapefruit because he failed, first, to palpate the abdomen, and second, to conduct a bimanual examination.

Genital Examination; Inspection

For the genital examination, the patient should be draped adequately with a clean sheet and placed in a lithotomy position, thus exposing the genitalia to inspection. A number of common conditions may be recognized by inspection alone, provided there is a good light, sufficient exposure, and an intelligent observer. Such lesions as verruca acuminata, pedicled tumor, kraurosis or epithelioma, as well as those conditions which result from childbirth injury—as cystocele, rectocele and uterine prolapse—immediately become obvious. Uterine prolapse may be obscured unless the patient is instructed to strain while the examiner separates the labia. Sometimes it is required that the patient stand with one foot supported on a low stool, and that she be asked to strain again when assuming a semisquatting position. Many cases of prolapse are overlooked by the examining physician because of the omission of the aforementioned procedures. Impairment of the urethral sphincter may be assumed if urinary dribbling appears when the patient strains. Genital abnormalities such as absence of vagina or septa, imperforate hymen and urethral lesions may also be discovered on careful inspection.

In my practice, the use of a *glove* on the examining hand, usually the left, has been so much a matter of habit that I feel

ulum which the Germans call "Spiegel," meaning mirror, is truly well named, for it imparts to the examiner's eye the accurate image of the exposed cervix and vagina. A speculum should be introduced with gentleness, should feel comfort-



Fig. 22.—An adequate gynecological office light. (Courtesy of Burton Manufacturing Company.)

able to the patient, and its use is predicated upon adequate illumination. After many years of searching for the proper *illuminator* that would shed the necessary light and still not be in the way, I found satisfactory a strong light on a stan-

teriorly, in order that the internal surfaces of both sacro-iliac synchondroses may be palpated. I have frequently discovered in women who complain of backaches and pains radiating into the thighs that no trouble was to be found in the genital organs, but that the pain could be reproduced by pressure over the inner surface of one or both sacro-iliac joints. External pressure over the tender joint will tend to confirm the

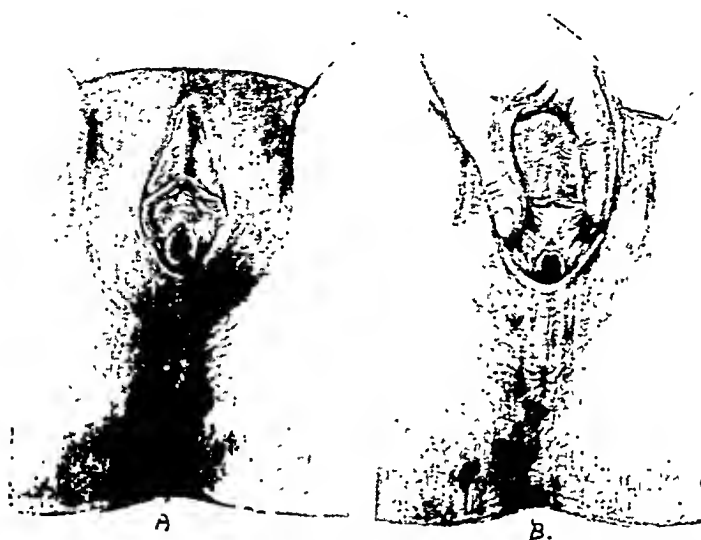


Fig. 21.—External urethral orifice. *A*, Nulliparous genitalia—orifice obscure; *B*, orifice readily visualized by spreading labia outward and upward.

diagnosis. Simple strapping of the back, application of heat, and a well-fitted sacro-iliac binder have cured many women who had thought they were doomed to semi-invalidism due to "female trouble."

LESIONS OF THE CERVIX

The cervix presents a variety of lesions, many of them extremely important from the standpoint both of diagnosis and the patient's future welfare. To differentiate them, however, requires more than mere palpation. The *vaginal spec-*

gonorrhea, *Trichomonas vaginalis* infections, and yeast infections of the vagina.

History

First of all, from the history one may suspect one or another of these conditions from the nature of the patient's complaints. If there is a history of recent exposure followed shortly by complaints of frequency and burning on urination and in a week or ten days by the presence of a smeary, yellow, sticky discharge, the impression one receives is that the patient has gonorrhea. One does not jump to a hasty conclusion, of course, but will then proceed to corroborate his suspicions. Secondly, if a woman complains that, immediately following her menstrual periods over a period of months, she has an intolerable itching in the vagina, chafing of the vulva and inner surfaces of the thighs, and a malodorous, profuse discharge, it is to be presumed that she is suffering from *trichomonas vaginitis*. Thirdly, if her complaint is mainly burning around the introitus, pain or soreness on coitus, with or without profuse discharge and itching, one would first think of a *mycotic vaginitis*. So you see that, from the history alone, one obtains leads which are valuable.

Inspection

Upon inspection, the patient with gonorrhea will have a smeary, sometimes crusting, yellowish or greenish discharge over the labia and, upon separating the labia, one observes redness of the mucous membrane of the introitus, with the redness particularly marked at the external urethral orifice and the orifices of Bartholin's ducts. The discharge one sees from the urethra and vagina is thick, yellow and of a creamy consistency. There is little or no odor.

In the case of *trichomonas vaginitis*, the labia and the creases of the thighs are usually red and sticky but there is no obvious crusting. There is a disagreeably acrid odor and, upon separating the labia, which in many cases are agglutinated, there is an outpouring of a thin, profuse, foul-smelling discharge containing small bubbles. This bubbly discharge is quite characteristic of *trichomonas vaginitis*. The introitus

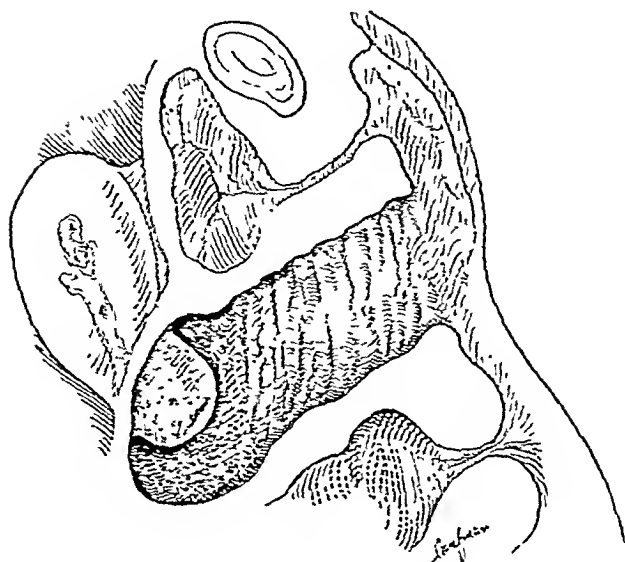
dard no larger than an ordinary microphone. The light can be projected horizontally through the speculum to give a clear view of the vagina and cervix. This light, which is inexpensive, can be obtained through your instrument manufacturer; it is called the *Burton light* (Fig. 22). It has been my experience that the little illuminating devices which are placed inside a speculum or attached to its rim are more in the way than useful, and reflected light from a head mirror such as is used by otolaryngologists is also unsatisfactory. Transillumination and colposcopy provide refinements of illumination that are rarely needed for routine accurate gynecologic diagnosis. I believe that careful palpation, good exposure and proper illumination are very important, but diagnosis depends most of all upon intelligent observation and interpretation.

In *virgins*, one ordinarily must forego both vaginal digital examination and inspection through a speculum. However, *recto-abdominal palpation*, which should also supplement the vaginal examination in other women, and, if need be, *vaginoscopy* by means of a small urethroscope or infant vaginoscope, such as I described some years ago¹ in connection with the treatment of vaginitis in infants, will be found very useful. (*Gynecography* is also extremely useful for those cases which present difficult diagnostic problems, but pneumograms required for this method of examination can rarely be obtained in office practice.)

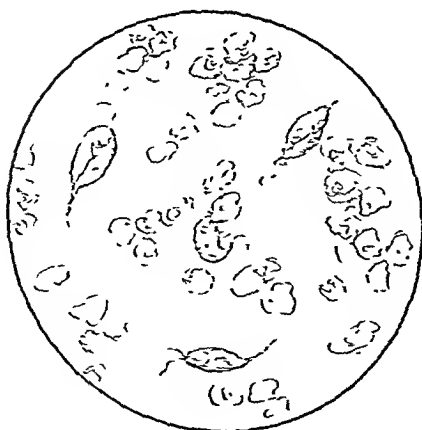
The vaginal mucous membrane should be observed as well as the cervix, and, when discharges are present, it is well to take *fresh smears* routinely from the vaginal vault by means of a wire loop or pipette (medicine dropper) for fresh hanging-drop examination. The value of this procedure will be brought out in the discussion of vaginitis. From the cervical canal, the material should be obtained on a cotton swab from which a thin smear is made for staining.

ETIOLOGICAL DIAGNOSIS OF VAGINAL DISCHARGES

In considering vaginal discharges, there are several significant leads which point to an ultimate diagnosis. Let us consider the three most common causes of vaginal discharge:



A



B

Fig. 23.—*Trichomonas vaginitis*. *A*, Appearance of portio and vaginal vault; *B*, trichomonads in fresh smear as seen under high power.

is uniformly reddened, and there is no particular accentuation at the glandular duct orifices, as is observed in gonorrhea.

In *mycotic infections*, one will find a very similar picture to that just described for *trichomonas vaginitis*, but there is usually a white, curdlike exudate adherent to the mucous membrane. While the discharge may appear somewhat similar, it is not as malodorous, nor does it always contain bubbles as in *trichomonas* infestations.

The *vagina* in gonorrhea is usually unchanged, for the gonococcus seeks out the glandular structures for its habitat, and merely uses the vaginal mucous membrane in transit. In *trichomonas*, one finds a strawberry-like appearance particularly in the vaginal vault and on the portio of the cervix. The bubbly discharge is especially profuse in this area. The *cervical canal*, which is the most common site of the gonorrheal infection, is unaffected by *trichomonas* inflammation, so that one may at sight practically differentiate these two common inflammatory lesions. A thick, mucopurulent, yellow discharge issuing from the external os of the cervix, with redness on the inner aspect of the canal, usually spells gonorrhea. A normal-appearing endocervix with clear mucus, associated with a reddened vaginal portio which is spotty, usually indicates *trichomonas vaginalis* infection. In yeast infections, the mycotic vaginitis, the same regions are infected as with *trichomonas*, the cervical canal being free. But the lesions differ from *trichomonas* in that there is a red, patchy erythema like a first degree burn, and frequently a white, curdy exudate is seen adherent to the mucous membrane of the vagina. The ultimate differential diagnosis of these conditions rests upon careful smear examination. In order that the diagnosis be complete, it is essential that both fresh smears and stained specimens be carefully examined.

Examination of Fresh Smears and Stained Specimens

A good routine for obtaining smears is to take a specimen with a cotton swab from the external urethral orifice and Bartholin's ducts, meanwhile exerting a slight pressure over

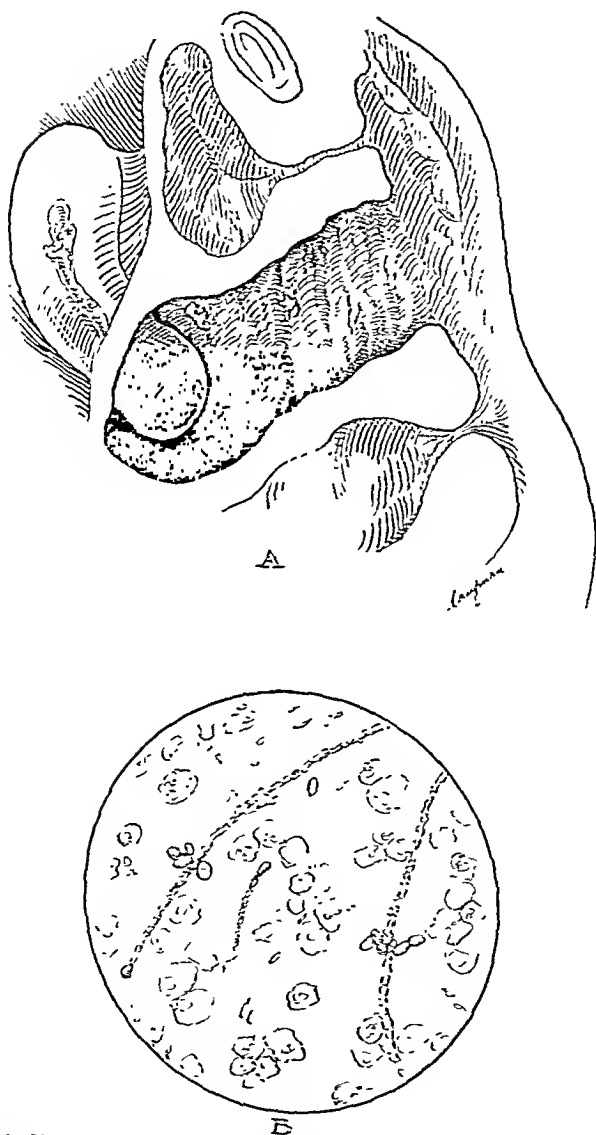


Fig. 24.—Yeast vaginitis. A, Appearance of portio and vaginal mucous membrane; B, mycelia and budding yeasts as seen under high power.

or under these structures to expel the exudate, and then to transfer this material to a slide for staining. Next, a speculum is introduced into the vagina, and material from the vaginal vault is transferred to a cover slip by means of a wire loop or pipette for fresh microscopic examination. It is advisable to thin the material on the cover slip with physiologic salt solution or distilled water (not tap water) so that the material can be observed in a hanging drop. Under the microscope one readily recognizes among the numerous pus and epithelial cells the oval, actively motile, nervous trichomonads, rapidly dodging in and out of the field (Fig. 23). Should yeasts be present instead of trichomonads, the general appearance of the smear is similar, but no activity is seen; here and there are the bamboo-like threads (mycelia) with buds along their stalks or at the end (Fig. 24). Where white patches are to be found on the mucous membrane, they should be removed by means of a wire loop, since this material usually contains the diagnostic mycelia and budding yeasts which can be seen both in the fresh and stained smears. Often the removal of the curdy patches will leave a slightly bleeding base.

From the endocervix it is best to take material by means of a cotton swab and to make a thin smear on a glass slide for staining. Gram's stain should be used for all specimens in which gonococci are sought, but, for the monilia, any aniline dye may be used. While ordinary low and high power are adequate for examining the smears of trichomonas and yeast, oil immersion should be used for detecting gonococci. The finding of one leukocyte containing the typical gram-negative diplococci in characteristic formation is sufficient to establish the diagnosis of gonorrhea. Slides which show many gram-negative cocci which are *atypical* and for the most part extracellular, as a rule indicate that the condition is not gonorrheal. Occasionally, one may observe a patient who has a chronic gonorrheal infection associated with trichomonas vaginitis, but in a three year study which I made some time ago, I found such association to be extremely rare.³ An infestation of *Trichomonas vaginalis* has frequently been observed *following* the successful treatment of gonorrhea.

provement. This usually occurs with three treatments, after which the patient is instructed to continue the douches at home until the next menstrual period. Immediately following the menses and before resuming douching, the patient should return to the office for a check-up of the smears. At this time it is advisable to give at least one additional treatment to prevent recurrence.

It has been my experience that, while *trichomonas vaginitis* is easy to relieve, it is difficult to cure, for recurrences are indeed frequent. A great deal has been written concerning the use of *silver picrate* powder or suppositories. However, I have never found cause to be enthusiastic about this form of treatment and stopped using it completely after observing a case of very extensive and intractable toxic dermatitis which occurred following the use of this preparation. Tablets of *lactic acid* and *kaolin* placed in the vagina have proved of value, as have some of the proprietary *beta-lactose* preparations. It is apparently important that the vaginal hydrogen ion concentration be reduced to about 4.5, and it is interesting in this connection to note that some of the contraceptive jellies now on the market, and which I believe to be very effective spermaticides, have been shown to have a hydrogen ion concentration of from 4.5 to 2.9; when used regularly, they should be useful in preventing these parasitic inflammations.

Treatment of Mycotic Vaginitis

In the treatment of mycotic vaginitis, I have found that painting the vulva and vagina with 1 per cent aqueous *gentian violet solution* and having the patient use *Lugol's solution*, 1 dram to each quart, as a douche, is successful in most cases. Some gynecologists use 5 per cent gentian violet in 40 per cent ethyl alcohol, but I have hesitated to use this because of the intense burning which it produces. One-fourth to one-half strength Lugol's solution has been painted over the vaginal mucous membrane, but this, too, is very irritating in many women who are sensitive to iodine. When gentian violet and iodine solutions have been used for a week or more, it may be necessary to change the prescription to an

TREATMENT OF VAGINAL DISCHARGES

The treatment for vaginal discharge obviously will vary in accordance with the etiology. I shall not take up the treatment of gonorrhea at this time since you all are familiar with both the older procedures and the newer developments in this field. I believe, however, that you may not be as familiar with the treatment of trichomonas vaginitis and the mycotic infections, and shall therefore discuss these briefly.

Treatment of Trichomonas Vaginitis

That there is no cut-and-dried, accepted treatment for trichomonas vaginitis is obvious from the numerous articles on this subject which have appeared in the gynecologic journals in the past decade. A perusal of these articles is likely to result in complete confusion. Nevertheless, the simplest procedures in some cases will lead to prompt and complete relief. In other cases which prove to be stubborn, recurrences appear after every menstrual period, and a succession of various treatments may be needed before the patient is free from this most obnoxious disturbance. One of the simplest remedies described is daily douching with 25 percent *sodium chloride solution*. Other substances have been used, such as *lactic acid*, 1 dram to a quart of water; *Lugol's solution* in similar dosage; and voluminous *plain water* irrigations.

In the average instance, I have found the most useful course to be a preliminary office treatment with *tincture of green soap* used liberally on the vulva and in the vagina, followed by an antiseptic wash of 1:1000 *potassium mercuric iodide solution*. After drying the vagina, a gauze pack soaked in plain *glycerin* is inserted which should remain in the vagina for twenty-four hours. Upon removal of the glycerin pack, a 2-quart douche of 1 per cent *lactic acid solution* should be used, and the patient instructed to take the douche lying down in the bath tub or over a bed pan. The patient should also be instructed to rinse the vagina thoroughly by alternately closing and opening the labia with the fingers while the solution is flowing, thus permitting alternate distention and emptying of the vagina. The office treatment should be repeated three times a week or until there is marked im-

In the routine office examination, as well as in the deliberate prophylactic check-up, the physician must pay particular attention to inspection of the cervix, keeping the early suspicious lesion in mind. It has been estimated that, of cancer

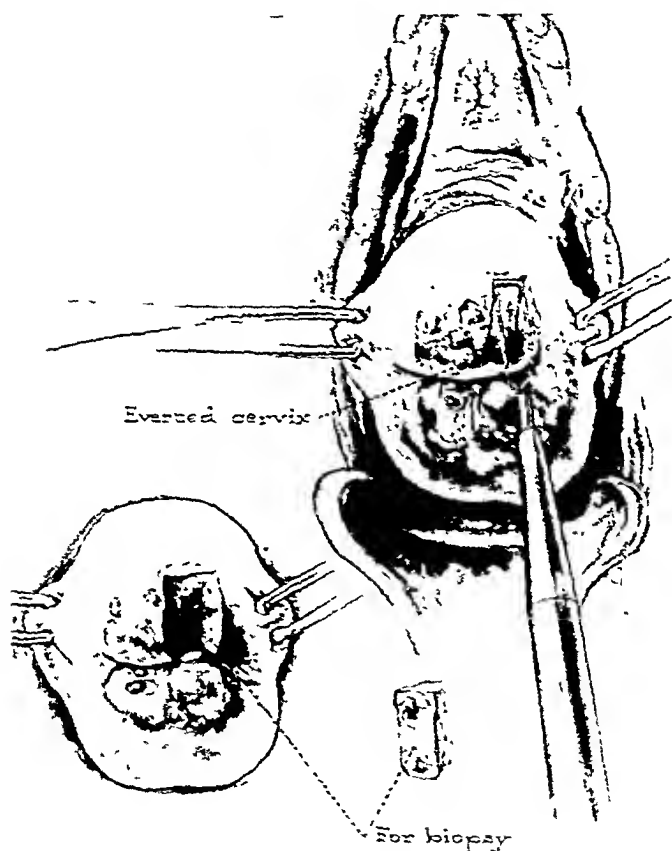


Fig. 25.—Biopsy of cervix. Author's method, employing rectangular endometrial loop.

deaths in women, one third are due to cancer of the uterus. Eighty to 90 per cent of these uterine carcinomas originate in the cervix, chiefly in the portio near the external os. The lesion thus is readily accessible and recognition of it in its

astringent preparation because of the local inflammatory reaction set up by the drugs used. In such instances, I have advised the use, twice daily, of 1:1000 *potassium permanganate* irrigations or *tannic acid solutions* (ordinary black tea).

CERVICAL BIOPSY

In the uterine cervix, the ordinary inflammatory lesions like simple erosion, ectropion and nabothian cyst formation can be disposed of readily by simple destructive cauterization with an ordinary nasal tip or solid-bladed cautery. However, for cervical biopsy, the tissue must be removed without too extensive coagulation in order to insure adequate diagnosis from the microscopic sections. This procedure may at times be performed in the office, provided the physician is equipped with a high frequency or endotherm apparatus, and the proper loops. Lesions which cause a suspicion of early carcinoma, granular erosions, and irritated areas about scars from previous childbirth should be subjected to biopsy. In addition, cervical polyps should be examined microscopically because of their tendency to undergo metaplasia. Endometrial biopsy has also become an office procedure for the gynecologist, and is used chiefly in sterility studies.

The most important function, by far, of cervical biopsy is the determination of the presence or absence of carcinoma. It is important that an adequate piece of tissue be removed from the suspected lesion; it should include a margin of healthy cervical tissue so that comparison can be made on the microscopic sections. Many physicians are of the opinion that such biopsies are best done in a hospital; however, they may safely be made an office procedure.

CARCINOMA OF THE CERVIX

Since carcinoma of the cervix is the most prevalent malignant tumor of the female genital tract and constitutes from one fourth to one third of all cancers in women, it is of paramount importance that its presence be detected as early as possible. It is primarily for this reason that I emphasize the importance of biopsy in the presence of a doubtful cervical lesion (Fig. 25).

made as an adjunct to the vaginal palpation, for only in this way can one distinguish clinically between the early localized lesion and the one that has extended to the parametrium, rectum and pelvic glands. Rectal palpation will also indicate whether the cervix is free or fixed in the pelvis.

Schiller Test and Colposcopy.—The Schiller test and the use of the colposcope may be found of material aid in establishing a diagnosis, particularly in cases of very early lesions. Schiller's test, which begins with the application of Gram's solution, is designed to discover minute lesions in the portio which are not yet characteristic macroscopic cancers. Small areas, even a few millimeters in diameter, which fail to take the iodine stain may thus be discovered. These whitish areas, which are in contrast to the brown-stained mucous membrane of the healthy portio, when biopsy is done may reveal the earliest stages of cancer, according to Schiller. However, clinicians are by no means in complete agreement as to the value of this test. Martzloff, in over seven years' experience with Schiller's test, has failed to discover a single carcinoma which he did not suspect by the usual methods; my own experience is similar.

Colposcopy is another means of discovering very early carcinoma, and, according to Hinselmann and some of his followers, it is the only means of detecting areas of beginning cancer. Again, however, some clinicians of large experience claim that they have failed to discover by means of the colposcope any beginning cancers or small lesions which were not perceptible to the unaided eye "after deliberate, thoughtful inspection."

These views should not, of course, discourage the use of the colposcope and the Schiller test, but rather serve as a warning against overconfidence in the results to be expected from their employment.

Obtaining the Biopsy Specimen.—A clinically recognized malignant lesion is at best only suspicious in character; histologic confirmation is required to establish a definite diagnosis. Biopsy is therefore imperative; an adequate piece of tissue, which includes not only a sample of the suspected area but of the adjacent normal tissue as well, must be re-

incipiency requires only that the physician be thorough in his inspection. Undoubtedly a large proportion of these deaths from cancer could be prevented by early recognition of the disease, for, in the early stages, cancer is curable. The cervix is in a vulnerable position for trauma; birth injuries, laceration, chronic inflammation—all are sources of irritation which may favor the development of cancer. During the reproductive period, women with childbirth injuries should be kept under surveillance and those with inflammatory lesions of the cervix should be treated with the specific means at hand. As menopause approaches, such lesions are looked upon with greater suspicion and may require more radical treatment. Cancer rarely develops after treatment of the uterine cervix, whether by cautery or repair, provided the offending lesion is completely removed and good healing ensues.

Diagnosis of Cervical Carcinoma

The diagnosis of frank cancer of the cervix is not difficult, and no special apparatus is necessary for its establishment, nor is it necessary to perform specific tests. Furthermore, every qualified physician should be able to recognize the characteristic lesion of malignancy if he will take the time and pains to make a thorough and intelligent examination. The diagnosis of cancer depends upon history plus palpation and inspection of the cervix. A *history* of intermenstrual bleeding, spotting on slight trauma, or of discharge which has become irritating or malodorous should always arouse suspicion, but it does not establish a definite diagnosis. *Palpation* which reveals a cervix that is enlarged, hard, irregular, and that bleeds on touch, is indicative of a well advanced carcinoma. However, even these factors are not sufficient without careful and intelligent *inspection*, with adequate exposure with a speculum and use of a good light. Then one may find the characteristically reddened, irregular, elevated and usually circumscribed lesion on the portio near or at the external os. Gentle swabbing with cotton usually elicits bleeding from the surface of the lesion. The growth may be flat, excavated or cauliflower in formation, and so friable that pieces break off readily. A *recto-abdominal examination* should always be

1. Epidermoid cancer (portio)
 - (a) Squamous cell type
 - (b) Transitional cell cancer
 - (c) Anaplastic cancer
2. Adenocarcinoma (usually developing within the canal)
3. Borderline conditions
 - (a) Benign hyperplasia
 - (b) Benign metaplasia
 - (c) Covert or precancers (these types may be noninvasive for months or years before giving real evidence of malignancy).

When the disease is limited to the portio, the prognosis is relatively good; cures may reach 52 per cent but only 20 to 25 per cent of all cervical carcinomas have a five-year salvage. According to Meigs, twenty per cent of the salvage in the first five years subsequently dies of carcinoma; even 4 per cent of the ten-year salvage eventually succumbs to the malignancy. Therefore it is improper to speak of five-year cures, for one must await the eventual death of the patient to ascertain whether cancer recurred before life terminated.

Prophylaxis

Prophylaxis is of course a most important field and one that gives promise for the future. We might say that, while there is no definite evidence that carcinoma is directly hereditary in the human, studies of case histories seem to indicate that a familial tendency is shown in 8 to 10 per cent of all cases of cancer. This fact, of course, should be kept in mind in dealing with lesions which might be construed as precancerous. There is justification for the claim that *semi-annual pelvic examination* for all women over thirty years of age is highly desirable.

While treatment of the cervical erosions by cautery and excision is not an all-embracing preventive, it nevertheless is prophylactic in the sense that it adequately reduces the percentage of women who would subsequently develop cancer from this source. As an example of this form of protection, Pemberton and Smith reported that, of 5962 women who had undergone amputation, cauterization or repair of the cervix,

moved for section. A biopsy specimen may be obtained by means of knife or scissors excision, punch, or cautery; in the opinion of the author, it is best obtained with a rectangular endotherm loop. The high frequency cutting current (so-called radio knife) permits a bloodless removal of an adequate block of cervical tissue without effacing the microscopic picture. It likewise is the method least likely to traumatize the lesion and thus favor the spread of cancer. The actual cautery is too damaging to the biopsy sample, while punch, scissors or knife is more traumatic than the endotherm loop. The current of the endotherm loop is sufficiently coagulating to seal the excision bed and thus prevent bleeding.

Examination of Frozen Sections and Paraffin Block Sections.—Having obtained a satisfactory block of tissue for diagnosis, the question arises as to whether an immediate examination of a frozen section should be made or whether it is wiser to await the results of the examination of permanent paraffin sections. If the specimen is sufficiently large, a small portion may be subjected to frozen section examination in order to obtain a provisional diagnosis, but errors in interpretation are likely, especially in early and borderline lesions, by this means. The gross topography of the tissue is all that one may expect to learn, leaving the study of cell structure and minute pattern to the more satisfactory paraffin sections. Paraffin block sections may be satisfactorily obtained in forty-eight hours, and multiple sections throughout the biopsy specimen may be studied, particularly the zone in which both normal and involved tissue may be seen side by side. The proper interpretation of biopsy material determines the course to be taken; hence, the sections must be studied by an expert pathologist! When doubt exists as to the exact nature of the lesion, multiple expert opinions may be required. Not infrequently, a lesion is seen which requires the utmost scrutiny and study before the examiner can reach a correct diagnosis.

Types and Prognosis of Cervical Carcinoma

Briefly, the types of cervical carcinoma to be found may be classified as follows:

cases with lymph node involvement for which radium would be ineffectual, a statement with which this author is in full agreement. Surgery, then, should at least be considered if the patient is a favorable risk and if metastases are not too extensive.

BIBLIOGRAPHY

1. Stein, I. F., Leventhal, M. L. and Sered, H.: Am. J. Dis. Child., 57: 120, 1929.
2. Stein, I. F.: Pelvic Diagnosis by Roentgen Visualization. Surg., Gynec. & Obst., 55: 207, 1932.
3. Stein, I. F. and Cope, E.: J.A.M.A., 22: 368, 1931; Am. J. Obst. & Gynec., 24: 348, 1932; *Ibid.*, 25: 819, 1933.

only five subsequently developed carcinoma. One might be inclined to conclude that only a total hysterectomy would serve as a complete prophylaxis for uterine carcinoma, but this measure is too radical to be advocated as a routine procedure and of course it carries with it a great risk of mortality and morbidity. Such radical measures should be reserved only for those patients with resistant cervical benign lesions who have a family history of cancer, and for those whose lesions show a tendency toward metaplasia.

Active prophylaxis ordinarily consists of general hygiene and hygiene of the genital tract particularly, plus eradication of chronic cervical erosions and deforming, incompletely healed lacerations of the cervix. For the treatment of *erosions*, cervical cauterization has proved to be most satisfactory. In extensive cases, conization by means of Hyam's endotherm loop may be advisable. Some authorities prefer complete endocervical excision by the Stürmdorf technic and still others a complete cervical amputation. The latter possesses the advantage of removal of the mucous membrane of the portio vaginalis in addition to the inflamed endocervix.

In order to reduce substantially the high mortality and morbidity associated with carcinoma of the cervix, a definite educational program must be followed which will impress upon women the necessity of *periodic examination*. When cancer is in its earliest stages, it can be cured, either by surgery or radium therapy. There should be no great difficulty in recognizing the lesions of early malignancy. A thorough, painstaking examination at the time of both routine and prophylactic check-ups may give physical findings of significance, and a history of intermenstrual bleeding, spotting on trauma, or persistent discharge, should arouse immediate suspicion which may be proved or disproved by biopsy.

Treatment

Radium therapy is the treatment of choice in cancer of the epidermoid type; however, when metastases have already occurred in the pelvis, its use is limited to palliation only. *Surgery* has proved of equal value in the early cases of cancer. According to Meigs, surgery will provide a cure in some

CONGENITAL HEMOLYTIC ANEMIAS

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Common Features of the Congenital Hemolytic Anemias.—

The different forms of congenital hemolytic anemia (familial hemolytic icterus, Cooley's erythroblastic anemia and sickle cell anemia) have many features in common. They are all characterized by jaundice, splenomegaly and anemia. The onset of symptoms is insidious and usually dates back to earliest childhood. *Pain in the upper abdomen* is a frequent complaint. This may be dull and rather fleeting in character or it may appear in the form of "abdominal crises." These crises often occur at night and are characterized by excruciating pain which may last for hours and which may simulate acute abdominal conditions. *Ulcers on the legs* are common in sickle cell anemia and in Cooley's anemia and may occur in congenital hemolytic jaundice.

All three conditions are characterized by *fluctuations* in the severity of symptoms. This is especially true in patients with familial hemolytic icterus who may have "hemolytic crises" during which they become acutely ill with fever, increased jaundice, increase in the size of the spleen and more marked anemia.

X-ray changes in varying degrees may occur in the skull and long bones, particularly in erythroblastic anemia and sickle cell anemia. The changes in the *skull* consist of thickening of the frontal, parietal, occipital and temporal bones with thinning of the inner and outer tables. In advanced cases, the

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at that time, was 2,850,000, the hemoglobin was 9.5 gm., the leukocyte count was 5200 and the differential count showed 84 polymorphonuclears, 15 lymphocytes and 1 monocyte. There was a slight degree of anisocytosis and poikilocytosis. Many of the cells were smaller in diameter than normal and lacked the normal central area of pallor. In a wet preparation, roulette formation was infrequent. When it did occur, some of the cells appeared distinctly thicker than normal. A few normoblasts and erythrocytes with nuclear remnants were present. The reticulocyte count was 4.8 per cent.

In spite of the apparent microcytosis, the mean corpuscular volume was 84.7 (Wintrobe method). The fragility of the red cells was increased. Hemolysis was very definite in the tube containing 0.58 per cent salt solution and was complete in that containing 0.36 per cent solution, whereas for the normal control hemolysis started in 0.44 per cent solution and was complete in 0.27 per cent solution. The icterus index was 15.6.

X-ray Examination.—X-ray films showed marked trabeculation at the distal ends of the long bones. The skull, however, was normal in appearance.

Pathology.—The spleen was removed on October 16, 1940, by Dr. Charles Sawyer. Dr. James W. Henry reported the pathology as follows: "The cut surface of the spleen is of a homogeneous, bright, brownish red appearance with prominent grayish-white corpuscular markings. The sinusoids are relatively empty, the sinusoidal endothelium standing out prominently. The pulp is packed with red blood corpuscles and, in areas, phagocytosis and hemosiderin laden macrophages are apparent."

Course Following Splenectomy.—On the day of discharge from the hospital, the red blood cell count was 4,130,000 and the hemoglobin 81 per cent. Today, the erythrocyte count is 4,640,000, the white blood count is 8950 and the hemoglobin is 78 per cent. The boy has lost his icterus, has gained in strength and weight and is a perfectly normal appearing individual. The reticulocytosis has subsided. Microspherocytosis is, however, still present.

Discussion

Familial hemolytic icterus is *hereditary*. In this particular case, only the mother could be examined. She had a hypochromic anemia of mild degree but did not present evidence of congenital hemolytic jaundice. In a more recent case, the

outer table may become so thin that it is invisible and the diploe become so prominent that they seem to extend beyond the outer table like the hairs on a stiff brush. The *long bones* show cortical thinning, widening of the shafts and medullary trabeculations.

The *anemia* varies in severity. It is usually mild and the erythrocyte count may even be normal if the amount and activity of the erythrogenic tissue are sufficiently increased. During hemolytic crises, the anemia may become quite marked. Characteristically, there is a high reticulocyte count. The white cell count may be normal but is usually elevated. The icterus index is increased and the van den Bergh gives an indirect or delayed reaction. The morphology and the fragility of the erythrocytes vary in the different types of hemolytic anemia and it is on this basis that the differentiation is made. These differences in morphology, in the fragility of the erythrocytes and in the treatment of the different types of hemolytic anemia are well illustrated by the following three cases.

CASE I. FAMILIAL HEMOLYTIC ICTERUS (CONGENITAL HEMOLYTIC JAUNDICE)

History.—The first case which we wish to present is one of familial hemolytic icterus. This boy, who is now five years of age, had a persistent mild jaundice from birth. At the age of three months, when first admitted to Mercy Hospital, he was found to have an erythrocyte count of 3,080,000 with a hemoglobin of 65 per cent. The spleen, at that time, extended 4 cm. below the costal margin. On three subsequent occasions, he was admitted to the hospital because of acute exacerbations of his illness. During these hemolytic crises, the anemia was more marked, fever was present and the jaundice was increased in intensity. On one of these occasions, May 31, 1940, the erythrocyte count fell as low as 1,480,000 with a hemoglobin of 25 per cent. The patient was tided over each of these acute exacerbations by means of transfusions, iron therapy and dietary measures. The spleen gradually increased in size and finally measured 12 cm. below the costal margin in the midclavicular line.

Blood Picture.—On October 14, 1940, the patient was admitted to the hospital in a period of remission. The erythrocyte count,

CASE II. COOLEY'S ANEMIA

History.—This little girl, who is twelve years of age, became our patient in an indirect way. Her older sister came to the Dispensary because of an ulcer on the right lower leg. Routine examination revealed a mild chronic anemia of the Cooley's type. We then requested the family to bring in Rose who was also known to have an anemia but was not considered to have any significant illness. The patient is of Italian parentage. She has from birth had a sallow, yellowish color and was discovered some years ago to have a chronic anemia.

Physical Examination.—On inspection, two features are outstanding. Skeletal growth is retarded and the facies is of a Mongoloid type, with prominent eyes and high malar eminences. The head is large with prominent frontal and parietal bosses.

The spleen is markedly enlarged, extending down well below the iliac crest. The liver is 5 cm. below the costal margin. There is moderate enlargement of some of the peripheral lymph nodes.

Blood Picture.—The erythrocyte count has varied between 3,000,000 and 3,500,000 and the hemoglobin between 7.0 and 8.0 gm. (40 to 50 per cent). The red blood corpuscles show extreme variation in size and shape. In contradistinction to the picture in pernicious anemia, however, the cells show definite achromia and the color index and mean corpuscular hemoglobin are well below normal. The mean corpuscular hemoglobin, as determined by the Wintrobe method, was 21.9 and the mean corpuscular hemoglobin concentration 24.5 per cent. There are four to ten normoblasts per 100 white blood cells and many cells with nuclear fragments. The reticulocyte count has varied between 3.7 and 8.5 per cent. The white count has never exceeded 9000. In contrast to the previous case, the fragility test shows an increased resistance (hemolysis began in 0.42 per cent salt solution and was complete in 0.2 per cent solution). The van den Bergh gave an indirect or delayed reaction and the quantitative reading was 1.66.

X-ray Examination.—The long bones show unusually prominent medullary trabeculation. This is most distinct in the small bones, the metacarpals and metatarsals. The total width of the bone is increased due to widening of the medullary portion, but the cortical portion is thinner and occasionally presents punched out areas. The skull bones do not show such marked changes. There is definite thickening of the bones but thinning of the tables is absent.

father, mother, two older brothers and an older sister were examined. The father and one brother had the disease in milder form. As a rule, the disease becomes manifest early in life. However, mild cases may escape notice until later in life and may then be considered "acquired."

The blood picture of familial hemolytic anemia is characterized by *spherocytosis*. Spherocytes are spherical erythrocytes which appear smaller than normal but which have a normal mean corpuscular volume. The cells look thicker than normal and lack the usual central area of pallor. In wet preparations, the normal tendency to roulette formation is disturbed.

The *fragility of the red cells* in congenital hemolytic jaundice is usually increased. Dameshek reports that some cells, during a hemolytic crisis, may have a decreased fragility so that hemolysis will not be complete until a lower concentration of salt solution than normal is reached. This combination of increased fragility and increased resistance during a crisis was observed in the above case. On June 3, 1940, hemolysis began in 0.54 per cent salt solution and was not complete until the tube containing 0.24 per cent solution was reached. The fragility test was repeated on June 5th with similar results. A trace of hemolysis occurred in 0.64 per cent salt solution and hemolysis was definite in 0.6 per cent solution. Hemolysis was not complete until the tube containing 0.22 per cent solution was reached.

As this boy illustrates, excellent results are obtained in congenital hemolytic jaundice by *splenectomy*. Patients are restored to good health although they retain the *spherocytosis*. Apparently, removal of the spleen prevents phagocytosis of the abnormally fragile red cells. There is some controversy concerning the proper time to perform splenectomy. We feel that surgery can be undertaken with less risk during a remission. If the patient is first seen during a crisis, transfusions, iron therapy and a diet providing all the essentials for red blood cell formation should be employed. Beneficial effects from *x-ray therapy* to the spleen have been reported, but such therapy brought about no improvement in this case.

was just palpable on deep inspiration. The liver could not be felt. Just above the ankle and overlying the tibia, there was a large, irregular shallow ulcer with sharp edges. Above this ulcer, there was a considerable area of more darkly pigmented, glistening, paper-thin appearing skin, the site of a previous ulcer.

Blood Picture.—At the time of admission, the patient's red blood cell count was 2,430,000, the white count 8750 and the hemoglobin 7.5 gm. or 43 per cent. The differential count showed 75 per cent polymorphonuclears, 15 per cent lymphocytes, 3 per cent eosinophiles, 1 per cent basophils and 6 per cent monocytes. There was marked anisocytosis and poikilocytosis. A few normoblasts and many cells with Howell-Jolly bodies were seen. In the stained blood smear, some oat-shaped and sickle cells were seen. In the hanging-drop preparation of fresh blood, many of the cells became elongated, filiform or crescent-shaped after standing four hours. The fragility test was essentially normal. Hemolysis began at 0.45 per cent salt solution and was complete in 0.3 per cent. The red cell sedimentation rate was 27 mm. in one hour (Westergren). The icteric index was 23. The reticulocyte count was 7 per cent, the bleeding time 3.2 minutes and the coagulation time 2.8 minutes. The urine showed no evidence of urinary tract pathology. The Kahn reaction was negative.

Sternal puncture revealed a very hyperplastic bone marrow with large numbers of normoblasts.

Course.—There have been marked fluctuations in the severity of the patient's symptoms. The ulcer has alternately healed and recurred. The erythrocyte count has varied between 1,900,000 and 4,100,000 but usually runs about 2,500,000. The hemoglobin fluctuates between 7.5 and 9.5 gm., the white count between 8000 and 15,000. Recently, the patient has been hospitalized. She has been given large doses of iron, vitamins and injections of liver extract. The ulcer has again healed and the patient has gained 17 pounds in weight. The spleen is no longer palpable.

Discussion

This case is so typical that it needs little comment. As Kracke states: "When a Negro presents himself with a marked anemia, splenomegaly and leg ulcers, the most probable diagnosis is sickle cell anemia." Only a few instances of the disease in the white race have been reported.

The sickle cell trait occurs in 7 to 8 per cent of Negroes. However, only 1.5 per cent of individuals with sickle cell

Discussion

Cooley's anemia is *congenital* but apparently not hereditary, although more than one case may appear in a family. The disease is peculiar to the Mediterranean races and has by some been thought to be due to chronic malaria.

The marked *aniso-poikilocytosis* seen in this case is characteristic. Usually, however, there are *many more nucleated red cells* (sometimes thousands per cubic millimeter). This erythroblastosis is the derivation of the name "erythroblastic anemia" so often applied to the condition.

In contrast to congenital hemolytic jaundice, the *fragility test* shows an increased resistance in most instances. Occasionally, the fragility may be normal.

The *Mongoloid facies* is typical of the more pronounced cases of this disease. Sometimes, there is even an epicanthal fold. Patients with milder disease may be perfectly normal in appearance and development.

The *treatment* in this type of congenital hemolytic anemia is *symptomatic*. Splenectomy does not have the beneficial effect that it does in congenital hemolytic jaundice. An adequate, well balanced diet, good hygiene and the administration of iron and liver help to maintain the patient in better condition.

CASE III. SICKLE CELL ANEMIA

History.—This young colored woman, aged thirty years, was first admitted to the Mercy Free Dispensary on October 6, 1937, complaining of an ulcer on the lower right leg. She states that an ulcer first appeared on this same leg twelve years previously, following slight trauma. The patient has never been robust and has, since early childhood, suffered frequently from headaches and vertigo. Measles, mumps and chickenpox were, however, the only specific illnesses experienced. There has been no surgery. Venereal disease has never been contracted. Menstruation began at the age of sixteen, was irregular in the beginning, but is now regular and normal in amount.

The patient's mother died at the age of thirty-seven years. The cause of death is not known. Her father, aged sixty-three, is known to be well. Her only brother, aged forty-three, is not in communication with her.

Physical Examination.—On physical examination, the spleen

THE IRRITABLE COLON

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COLONIC dysfunction is the chief cause of abdominal pain or discomfort. For many years colitis was used to designate colonic irritation. Sippy very early recognized that this term was not a proper one and used the designation "irritable colon" to describe such a noninflammatory disturbance. While I served as his assistant, my interest in this type of colon dysfunction was stimulated and the fundamentals emphasized in this paper were learned.

ANATOMY AND PHYSIOLOGY

A knowledge of the anatomy and physiology of the normal colon is necessary for a fundamental understanding of the symptoms and treatment of an irritable colon. It is not within the scope of this discussion to describe in detail the anatomy. Morgan¹ stated that the *nervous mechanism* of the colon is maintained by a balance of tonus between the vagus and the sympathetics and that local control is through Auerbach's and Meisner's plexuses. The normal physiology has been explained in a thorough manner by Laus². With an understanding of the colon in its normal state one can appreciate the importance of the time element in the progress of material through the gastro-intestinal tract in this very common condition.

Adler, Atkinson and Ivy³ have recently reported a very interesting study of the *motility* of the human colon. They observe that under certain conditions the disorganization of the types of motility of the colon may be increased, and the syndrome of so-called "spastic" or "unstable" colon may occur in the absence of easily recognized roentgenologic evidence.

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develop anemia (Sydenstricker). According to Taliaferro and Huck, sickle cell anemia is inherited as a Mendelian dominant.

In a stained smear, the outstanding feature is the marked *aniso-poikilocytosis* and very few sickle cells may be seen. However, when a sealed preparation of fresh blood is allowed to stand, the cells become elongated, filiform or crescent shaped (*sickling test*). The length of time required for sickling to occur will vary from time to time in the same individual. As is the case in all hemolytic anemias, the bone marrow is hyperplastic and the peripheral blood is flooded with large numbers of young cells.

The *fragility test* in sickle cell anemia does not, as a rule, show any departure from normal, thus helping to differentiate the condition from other members of the group.

The *spleen* is usually enlarged early in the course of the disease, but, after the condition has existed for some time, it gradually shrinks in size until it is no longer palpable.

The condition is a chronic one and those afflicted usually die from some intercurrent disease. Mason states that sickle cell anemia has never been reported in individuals past thirty-five years of age, although the sickle cell trait has been observed as late as seventy-eight years.

Treatment is very unsatisfactory. Splenectomy may give some benefit early in the disease when the spleen is still enlarged. Later it is definitely not of value. Intensive anti-anemic therapy is of no avail. The ulcers are also very resistant to therapy but may respond to prolonged bed rest.

Diet

Diet may be an etiologic factor when it becomes excessively irritating. The normal colon will tolerate a great deal of irritation without manifesting it by abdominal distress. Healthy individuals have occasional bouts of pain after dietary indiscretion, but there is usually a rapid recovery. It is after these indiscretions are repeated that the various dietary fads are tried. After one is tried, another is suggested and usually many have been followed. Finally the colon becomes so irritable that almost all foods cause some discomfort. A most satisfactory result can be obtained in this type of irritable colon if the proper treatment is followed.

Emotional Upsets and Other Factors

Colon irritation as a result of *emotional upsets* is common. It is easily seen that this may include a multitude of conditions, few of which can be discussed at this time, but family troubles, anxiety, fear, and frustrated social ambitions have to be considered in the successful management of an irritable colon.

Other etiologic conditions are *migraine*, *chilling of the body*, *allergy*, *menopause*, *hyperthyroid* and, more often than is generally recognized, *hypothyroid states*. Inflammatory conditions such as gallbladder disease and appendicitis may initiate colon irritability, but in my experience they more often aggravate a preexisting irritation. Over a period of years it has not been my observation that rectal disease alone causes abdominal pain.

CLINICAL PICTURE

The clinical picture in irritable colon is fairly definite. The most frequent complaint is a *distress* rather than a pain; however, it can be extremely painful. The site of occurrence is usually in the lower abdomen, but it may occur any place in the abdomen. In pointing out the site of the distress the patient usually passes his hand across the abdomen or follows the course of the colon. It is intermittent in type, varies in place of occurrence, occasionally radiates, and is accompanied by a feeling of distention or fulness. *Rumbling* and

ETIOLOGY

The etiologic factors are legion, if everything that upsets normal physiology is considered. However, there are a few very common causes that can be explained.

Cathartics

My experience over a period of twenty years corroborates that of Collins and Van Ordstrand⁴ who found that cathartics play an important part in most of the cases. A well taken history reveals that the patient failed to have a bowel movement and, after waiting twenty-four to forty-eight hours, became alarmed and took a "strong" cathartic. This was followed by the passing of many stools, usually of watery consistency. After this he did not have a bowel movement because the colon was seeking to establish its normal function. The cathartic was repeated and changed until many kinds were taken over a period of months and years.

After taking such punishment for a long time the colon becomes so irritable that a typical distress develops and causes so much discomfort that the patient seeks medical advice.

Enemas

The use of enemas, although probably not so common, causes a similar reaction. Small enemas are employed and if "sufficient" results are not produced, the size is increased and various kinds of irritants are introduced. The rectal tube is inserted to a higher and higher level in order to get a "high enema." Various positions are assumed in order to empty the "whole bowel." Colon irrigations are not infrequently taken. It is surprising the amount of fluid a patient will use after he has become addicted to colon irrigations. One patient has come under my observation who used twenty-two gallons of salt water once a week in order to get a "thorough cleaning." Enemas may cause such a severe irritation that large quantities of mucus are passed in the stools. The mental reaction of the patient to large quantities of this mucus is at times astounding and an apprehension neurosis may develop, especially if he is not properly advised. It should be generally recognized that mucous surfaces pour out mucus to protect irritated membranes.

ination of this stool reveals clostridia. In my opinion the bacteriologic examination of the stool only occasionally reveals anything of clinical value in an uncomplicated irritable colon. Blood in the stool is not a part of the picture in this syndrome. *Mucus* in varying amounts is very common.

X-ray Examination

X-ray examination is routine, but it is not as important as it is in the presence of organic disease of the colon. It should be understood that filling the colon with barium may increase the irritation, consequently the examination should not be started until all other diagnostic work is completed. The preparation for the examination differs from that followed when organic disease is suspected. A cathartic should not be given to empty the colon, since the one cathartic that is most likely to empty the whole colon is certain to increase the irritation. An enema made with one pint of warm water is sufficient.

Fluoroscopic examination is of most diagnostic value. As the barium enters the colon, contractions due to spasm may be seen which cause the haustrations to disappear. The colon may be finger size, but will fill to normal size as the enema is continued. Not infrequently the patient, to indicate the site of pain, will point to the area where the spasm is seen and state that the pain "is gone" when the spasm relaxes. Pain caused by the barium enema is relieved by expulsion of the barium, provided enough is expelled.

Differential Diagnosis

Diagnosis of irritable colon is made by *exclusion*, not on direct or positive findings. Other gastro-intestinal disturbances should be ruled out first. It should be generally recognized that no other abdominal organ is likely to cause pain of daily occurrence over such a long period of time. Distress caused by a *peptic ulcer* is more localized, constant, has a definite time element as a rule, and is relieved by food or sufficient alkali to neutralize the free hydrochloric acid present. Roentgen ray examination of the stomach will reveal the casual lesion.

gurgling, nausea, passing of flatus, and occasionally a *burning sensation* across the center of the abdomen are not infrequently a part of the clinical story. The time of occurrence may be at any time if the colon irritation is of long standing but is usually while eating or very soon after the meal. It has been frequently explained that the gastrocolic reflex is responsible for the latter. It may occur during the night but this is rare and I am inclined to suspect some other cause when the patient is awakened in the middle of the night by abdominal pain. The distress does occur soon after arising and is not relieved by eating breakfast.

Belching is a common complaint and becomes a bad habit which is difficult to overcome. Because by belching a relaxation of pressure on the colon is obtained, the patient encourages the habit. It may at times be necessary to carry the patient through a complete gastro-intestinal routine in order to prove to him that there is no gas in his stomach.

DIAGNOSIS

Physical Examination

Physical examination should be carefully and thoroughly done in order to rule out any other condition. An irritable colon will cause a *tender* colon which in its descending portion can be rolled under the palpating finger like a rope. Superficial muscular tenderness may be misleading. This can be more accurately determined by having the patient lie on his head and heels while the abdominal wall is lifted or pinched.

Laboratory Findings

The laboratory findings reveal a negative blood count except for a rather frequent low hemoglobin. *Urine* examination is negative. Inspection of the *stools* may reveal helpful information. The form and consistency should be noted. The ribbon-like and finger-size stools indicate a spastic condition. However, hard-formed or mushy and watery stools may be seen in the presence of a highly irritable colon. A stool that is mushy, full of bubbles, acid to litmus, and has a butyric odor occurs when there is fermentation. Microscopic exam-

1. Patients with "Constipated" Stools

Constipation is diagnosed on the basis of hard-formed stools that are difficult to expel, whether the condition occurs daily or irregularly. The popular treatment for such a patient is to allow plenty of vegetables and a large quantity of fruit. Again my experience agrees with Collins and Van Ordstrand that such a diet is contraindicated. In the observation of more than 3000 cases, a *low residue diet*, omitting all fruits, and the use of 2 to 4 ounces of warm oil as a *retention enema* each night until the distress has definitely improved, have given the best results. An *evacuation enema* made with not more than 1 pint of warm water may be used if necessary.

As the distress improves, one vegetable at a time may be added. When the distress is not troublesome and the stools are not soft formed, fruit may be added and is tolerated better after taking food than before. It should be understood that no one diet will be satisfactory for all patients. As a rule, corn, cabbage, cucumbers, sauerkraut and highly seasoned foods are most irritating and should be added cautiously, if at all. All cathartics are forbidden.

2. Patients with Normal Stools

The dietary management of this type is not as a rule difficult. It is usually possible to start with the bland foods and one to three cooked vegetables daily, such as string beans, spinach, asparagus and carrots, omitting any vegetables that the history may have indicated as irritating. Baked beans, sweet potatoes, peanuts and lima beans are omitted if the passing of flatus is a complaint. Additions are made as the distress lessens. It is usually necessary to use heat on the abdomen and to administer an antispasmodic drug.

3. Patients with Watery Stools

The patient with an irritable colon who is having mushy or watery stools is given small feedings at two-hour intervals, consisting of gruels, boiled milk, poached or soft boiled eggs, and milk toast. As the diarrhea improves, other bland foods are added and three meals daily are allowed. As the stool

Chronic gallbladder disease may challenge the ability of the most skillful diagnostician. It should be borne in mind that the presence of gallstones does not necessarily mean that they are causing symptoms. In the acute attacks of gallbladder disease the severe, localized pain with localized tenderness and muscular rigidity are helpful. It also has an inflammatory background, the evidences of inflammation being a rise in temperature and leukocytosis. The gallbladder dye may help.

In *acute appendicitis* there is a sudden onset with a definite severe pain. In most cases there is also localized tenderness and muscular rigidity, elevated temperature, and leukocytosis. It is certainly being more generally recognized today that *chronic appendicitis* is not of frequent occurrence. If more attention is given to the diagnosis of irritable colon, chronic appendicitis will become a comparatively rare diagnosis.

Genito-urinary disease can be ruled out by a carefully obtained history, which should not be a forgotten art, and the necessary investigative procedures. *Organic disease of the colon*, such as polypi, carcinoma, ulcerative colitis and other ulcerations may be complicated by the picture of an irritable colon but they can be diagnosed if the history, proctoscopic examination, stool examination and roentgen findings are carefully evaluated.

In *migraine*, the classical history is usually obtained, and in *hypothyroidism* the slow pulse, nail changes, blood pressure, dry skin, speech and metabolism should make the diagnosis very definite.

MANAGEMENT

If the patient with irritable colon is seen reasonably early, its management may be easy and satisfactory results are the rule. Some of the very late cases will challenge the ability and patience of the most expert. *Diet* is the fundamental part of the treatment.

It seems to me desirable to classify patients who appear for treatment into three types: (1) those with "constipated" stools; (2) those with normal stools, and (3) those with watery stools.

3. A method of treatment that has given satisfactory results was outlined.

BIBLIOGRAPHY

1. Morgan, W. S.: Etiology and Treatment of Spastic Colon. *Southern M. J.*, 20: 380-382 (May) 1927.
2. Laus, Clark J.: The Irritable Colon Syndrome. *Radiology*, 24: 572-590 (May) 1935.
3. Adler, Harry F., Atkinson, A. J. and Ivy, A. C.: A Study of the Motility of the Human Colon. *Am. J. Digest. Dis.*, 7: 197-202 (June) 1941.
4. Collins, E. N. and Van Ordstrand, H. S.: *Cleveland Clinic Quarterly*, 8: 67 (April) 1941.

becomes soft formed, vegetables are added. Fruits are usually added last.

The antispasmodic drugs are of definite help in most cases, e.g., *tincture of belladonna* in doses of 10 to 20 minims three to four times daily. It is recognized that the tolerance for this drug varies widely in different individuals, but in my experience large doses for a short time give a better result than small doses for a longer period of time. *Trasentin* will give satisfactory results in many cases. In the mild diarrhea, *tannagen*, grains 10 three to four times daily, and *kaolin* with or without *amphogel* may be used. Sippy used a combination of *calcium phosphate*, *calcium carbonate* and *bismuth subcarbonate* in 60-grain doses; this is effective in a large number of cases. For the irritable colon accompanied by a stubborn diarrhea, *paregoric* or *tincture of deodorized opium* may be used with satisfactory results. It must be understood that the opium preparations are habit forming. *Bromides* in 10 to 15 grain doses and the *barbiturates* in small doses are helpful in all three types to control the nervous reactions.

Emotional individuals, or those who have been commonly called *neurotics*, will require a studied application of what was at one time called the art of medicine. When properly used it will suffice in most cases, but much patience is required. Rarely there may be a psychiatric problem. If so, it is best to refer the patient to a competent psychiatrist, and in my experience a satisfactory improvement has usually resulted.

It is generally recognized that the individual with an irritable colon who remains on a restricted diet for a long time should be given sufficient vitamins to assure him the recognized daily requirement. Vitamin C should not be forgotten.

CONCLUSIONS

1. A knowledge of the anatomy and physiology of the normal colon is essential for a fundamental understanding of irritable colon.
2. The etiologic importance of cathartics, enemas and diet was discussed.

3. A method of treatment that has given satisfactory results was outlined.

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COMMON DISEASES OF THE RESPIRATORY TRACT IN INFANTS AND CHILDREN

ARTHUR F. ABT, M.D.*

THE COMMON COLD

THE common cold is by far the most frequent infection encountered in infancy and childhood. It is an infection which leaves no immunity and tends to recur with varying frequency in the individual. The child of school age can be expected to have one or two colds a season.

The common cold is highly contagious, and the incubation period is relatively short. The etiologic agent is a filtrable virus, and bacteria which are common inhabitants of the respiratory tract act as secondary invaders. Infants are most commonly infected either by adults or older children in the home. Young children, when they start to kindergarten or school, are commonly afflicted and on occasions spend more time at home than attending school, because of colds. The older school children, after the age of eight or nine years, are less frequently affected.

The common cold itself is more or less a self-limited infection. It is important, however, because it leaves a path for *secondary invasions* of the nose, nasal sinuses, ears, mastoids, pharynx, larynx, trachea, bronchi and lungs. Most of the symptoms and diseases to be here discussed are sequelae of the common cold.

The relationship of the *tonsils* to the child's susceptibility to colds has been studied, and in general the child whose tonsils have been removed follows the same course as a nontonsillectomized child.

The *frequency of incidence* of colds rises steeply and remains at a high level from the ages of about four to eight

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use of ice-cold sprays and daily periods out of doors, no matter what the weather.

In my experience, there seems to be a *familial susceptibility* and *resistance*, which varies considerably from family to family, and from child to child. The most susceptible infants in my experience are those whose parents are continually catching colds and passing them on to their offspring. It sometimes takes considerable patience and a great deal of tact to

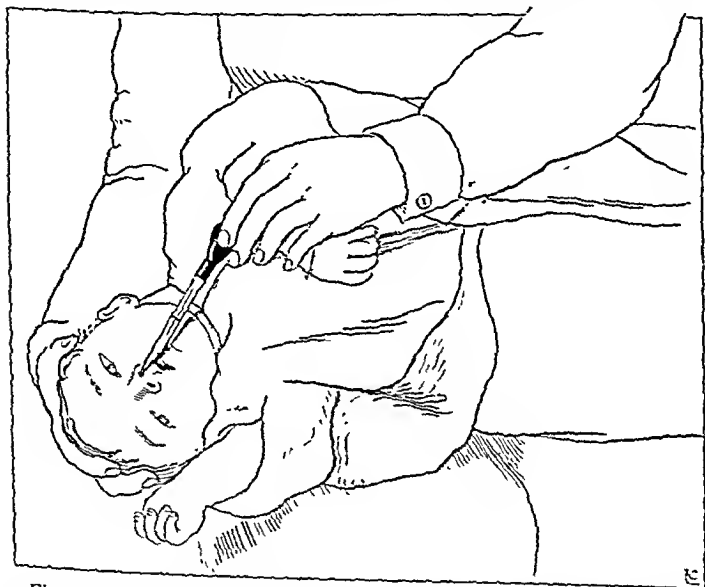


Fig. 26.—Application of nose drops in the young infant. The head-low posture is employed, the child being held over the lap. Non-oily drops are employed.

convince an offending parent that he or she is the source of the family colds, and to institute the proper prophylaxis which such a situation requires.

The remainder of the treatment of the common cold is symptomatic. *Fluids* should be freely given and the *diet* limited, if fever is present. *Antipyretics* and *sedatives* have their place. A *proper humidity* in the sickroom is often an aid and relieves the dryness of the nose and throat. *Mild vapors* may be used.

years; thereafter the cold incidence drops each season, until between the ages of ten and twelve years and thereafter the child usually has one or two colds a season.

Treatment

In the treatment of the common cold, the most important measure is to keep the individual *quiet* and *in bed*. With young infants this is no problem. However, with the run-about child, it is often a difficult procedure. Many mothers look askance when told that the best treatment for their child's cold is to keep him in bed. Keeping the child in bed serves at least two purposes: it keeps him at an even temperature, and from further chilling if he has fever; secondly, it keeps him isolated and away from other children in the family and thus prevents spreading disease throughout the household. I have noted in my practice and in my own family that if the infant or child is kept in bed at a fairly even temperature, the course of the infection is shortened and the liability to unpleasant sequelae is reduced.

One often encounters in practice certain difficulties in this regimen. In certain families the doctrine of fresh air treatment for colds is the rule; among other families the hot, dry air theory is practiced, the child being kept in a small room with the radiator wide open, the temperature 85° to 90°, the windows tightly closed and three or four blankets on the bed. Following a call to such a home, the visiting physician in a lather of sweat draws a deep breath of fresh air on the doorstep and wonders how prehistoric children were treated before the advent of steam heat. One frequently encounters the "physic-ing" mother, though I could never comprehend how she would check the nasal coryza by intestinal catharsis.

All school teachers are familiar with those parents who don't believe in colds and are persistent in sending their children to school with fever, coryza and cough; these are the children who spread the infection through the kindergarten and school, and according to their parents are never sick until they just can't get up and walk.

A final group might be mentioned—parents who believe in hardening their offspring to the rigors of the climate by the

Administration of Nasal Drops.—The practice of applying oily nose drops has met with disfavor because of the possibility of producing a lipoid pneumonia, which shall be discussed later. The proper method for administering nose drops to both infant and child is illustrated in the accompanying figures (Figs. 26-29).

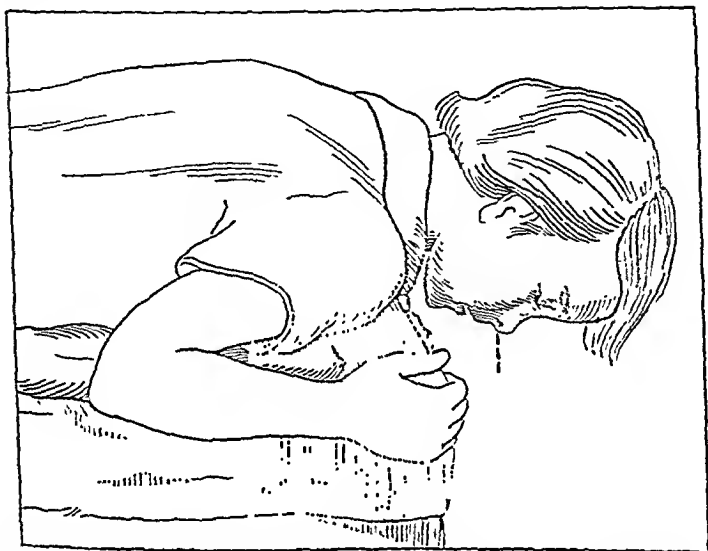


Fig. 29.—The child lies on the abdomen and facilitates the drainage of nasal secretions, following the lateral head-low position.

COUGH

Cough in the Newborn

Cough is not a usual symptom in the newborn. Its occurrence suggests some *congenital anomaly* of the respiratory system. Cough might be one of the symptoms of a congenital pneumothorax. Congenital cyst of the larynx may cause cough and asphyxia in newborn infants.

Atelectasis in the newborn period or in early infancy may be evidenced by cough; the atelectasis may be due to an obstruction of the main bronchus or to obstruction of many finer bronchioles, and is frequently mistaken for a basal pneumonia. X-ray examination reveals a triangular shadow at

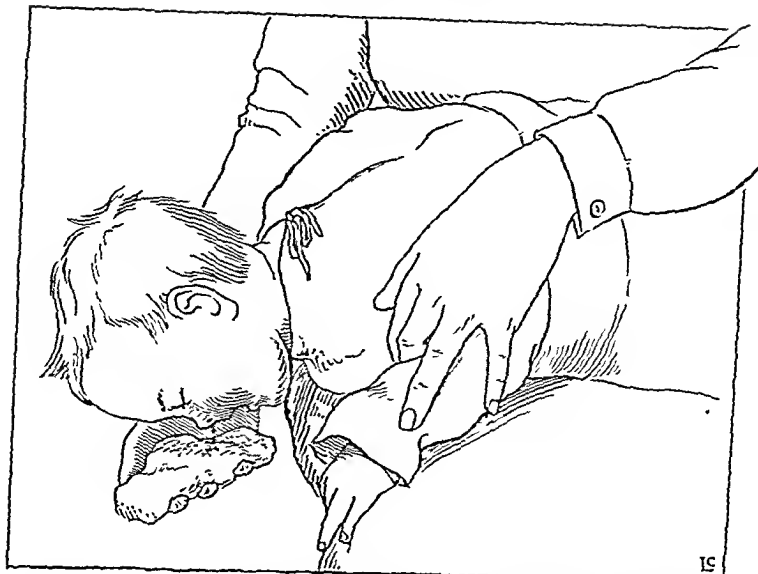


Fig. 27.—Two to three minutes after the drops have been inserted the infant is turned face downward, allowing the nasal contents to escape from the nostrils. Following this technic, none of the solution enters the throat or is aspirated.

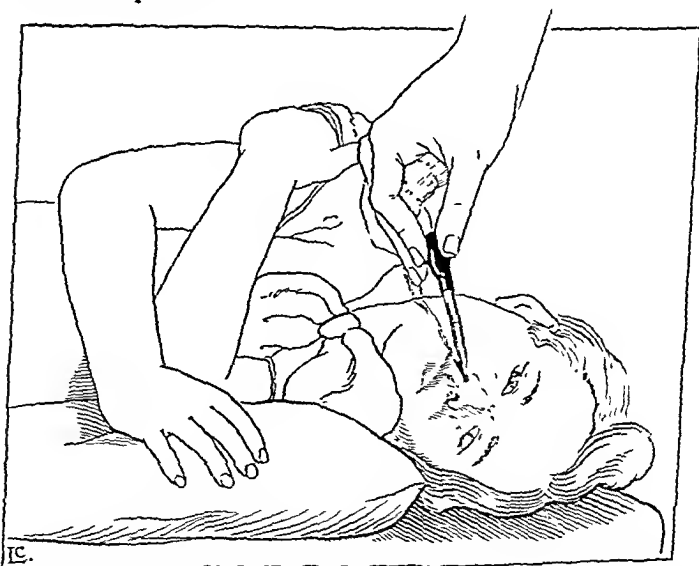


Fig. 28.—Instillation of nose drops in older child, using the lateral head-low position. A pillow under the shoulder facilitates the technic. Vaso-constrictor drugs in an isotonic solution are used.

followed by whooping is characteristic of pertussis in older children, although it is rarely heard in infants with the disease. The *raw, barking croupy cough* which comes from the larynx, once heard, is readily recognized. Another typical cough is the *bellowing* type which originates in the trachea and which is common in children with an ordinary cold.

When due to inflammation or mechanical irritation, the cough will be *dry*; if there is secretion, it will be *moist*. The dry cough often occurs in a chronic condition, where the coughing does not remove the cause of the irritation. In such cases, treatment of the irritation, rather than the cough, is indicated. On the other hand, when the cough does fulfill a purpose, such as removing secretion, it is often a grave mistake to relieve the cough through the use of codeine or other sedatives.

EPISTAXIS

Epistaxis in the Newborn

Epistaxis is uncommon in the newborn and young infant. A serosanguineous secretion from the nose is often an early sign of *congenital syphilis* in infancy. *Nasal diphtheria* should also be considered in an infant who has a continued sanguineous mucopurulent discharge from the nostrils. *Telangiectases* of the mucous membrane or *nasal polyps* may also be the source of epistaxis in the infant.

Epistaxis in the Older Child

Epistaxis is a much more common symptom in the older child. The most usual cause is some *local irritation*, a blow, a fall on the nose or an internal irritation of the nasal mucous membrane from picking the nose. Occasionally, children insert *foreign bodies* in the nasal passages, and irritation from such a source may cause epistaxis. Frequently, after an acute cold a small *ulcer* on the nasal septum will bleed freely after blowing of the nose.

Epistaxis may be a *prodromal symptom* of many systemic diseases, as typhoid fever, scarlet fever, measles and septicemia. The older writers paid special attention to epistaxis as a prodromal symptom of acute rheumatic fever. It has been said that epistaxis occurs in nearly one-quarter of those rheumatic

the base of the lung. The cough usually persists after the pulmonary symptoms have abated, and x-ray examination reveals the persistence of the triangular shadow. If the condition persists, it will be noted in later examination that bronchial dilatation is developing and a case of bronchiectasis is liable to develop, with persistent chronic cough. Treatment in an attempt to prevent the development of bronchiectasis should be begun early, after the persistent cough and the typical triangular shadow at the base of the lung have made the physician aware of the condition. Postural treatment, with the infant prone and the head down, may be instituted. Bronchoscopic aspiration, if performed early, may effect a rapid cure.

Cough may be a symptom of infections of the upper respiratory tract in infancy. During *grippal epidemics* newborn infants often contract a rhinopharyngitis of which cough may be a prominent symptom. A mother afflicted with *pertussis* near term may transmit the disease to the offspring. Persistent rhinitis and cough in early infancy should make one suspicious of *congenital syphilis*.

Pneumonia in the newborn may be asymptomatic; cough and fever may be absent. Failure to properly clear the air passages of the newborn infant, or aspiration of amniotic fluid, may lead to the development of a pneumonia. Aspiration of oily substances may cause so-called "lipoid" pneumonia; this will be discussed more fully under pneumonia.

Cough in the Older Child

Cough denotes irritation caused by respiratory disease and is perhaps the most frequent sign which brings the child to the physician. It should be remembered that the cough is a reflex, which should be regarded as a defense reaction against invasion of the respiratory tract by a foreign body. The origin of the cough may be in any part of the respiratory tract, or it may originate by indirect stimulation from neighboring anatomic structures, such as the enlargement of the bronchial glands at the bifurcation of the trachea.

The sound and character of the cough may aid the physician in locating the nature of the illness. The *staccato cough*

ACUTE LARYNGITIS

Acute laryngitis is often associated with rhinopharyngitis. It may be the primary lesion, though it usually extends downward from the initial infection in the pharynx. Laryngitis caused by pyogenic bacteria is often a complication of the infectious diseases, especially *measles*. *Diphtheritic laryngitis* should always be ruled out clinically, and if there is any doubt, valuable time should not be lost in waiting for bacteriologic culture reports. It is imperative to give diphtheria antitoxin as early as possible, and the physician who gives diphtheria antitoxin early ten times in cases of acute laryngitis which eventually turn out not to be of diphtheritic nature, will have no regrets; while the physician who hesitates once with an acute laryngitis, waits twenty-four hours for one culture and twenty-four hours for another culture, will sorely regret, when a diagnosis of diphtheria is finally established, that he did not give the antitoxin early.

The chief symptom of acute laryngitis is a *hard, rasping cough*, although *hoarseness* may be the only complaint. It is seldom that the child complains of external pain over the larynx.

Treatment

The child should be put to bed and kept in bed. The room should be kept at a warm, even temperature. Dry, cold night air usually is irritating and ventilation should be confined to the interior of the home, leaving the room door open if necessary. As acute laryngitis usually occurs in the winter-time when the humidity is low, it is advisable to add moisture to the air. The humidity may be considerably increased by simply hanging up wet towels or sheets in the room. Excellent results may be obtained by modern mechanical humidifiers. Antiseptics may be administered in appropriate doses, as eucalypti or ephedrine and salicylate like the bromides and barbiturates are useful. The use of atropine or its derivatives is contraindicated as the drying effect on the mucous membrane tends to aggravate the condition.

patients with uncompensated heart disease whose symptoms are noted over a number of years.

In *blood diseases* such as simple purpura, thrombopenic purpura and the acute leukemias, epistaxis may be a premonitory symptom. I have never seen epistaxis manifest itself as a symptom of scurvy in infancy, though it may occur in the older individual afflicted with scurvy. In the hemorrhagic or purpuric forms of certain febrile diseases, such as meningococcemia, nasal hemorrhage may occur. *Variations in atmospheric pressure*, such as change to high altitude, may be the cause of epistaxis. Finally, in young girls epistaxis may precede the *menstrual flow*. Usually such epistaxis is associated with ulceration of the nasal septum.

Occasionally bleeding from the nose may be overlooked and cause difficulties in diagnosis, if the blood runs backward into the pharynx and is swallowed and there is no evident anterior bleeding. In such a case a child might vomit clotted blood and if the nasal passages were not thoroughly examined for the source of the bleeding, a mistaken diagnosis of gastric ulcer might be made.

Treatment

In the treatment of simple nose bleed the child should be placed *at rest*. Ice may be placed over the nose and cold may be applied to the back of the neck, thus exciting reflex contraction of the capillary vessels. Local applications of solution of *adrenalin* or *ephedrine* ointments may be necessary. *Sedatives* may be required to quiet the child. If the local measures fail, it may be necessary to *pack the anterior or posterior nares*. In bleeding due to systemic and not local causes, *human blood serum* or *whole blood* injected intramuscularly may remedy the condition. In very severe hemorrhages *blood transfusion* may be required. Ulcers of the nasal septum may be touched with chromic acid solution, or chromic acid fused on a probe and thereafter vaseline or some simple ointment may be applied to prevent the formation of crusts and further irritation.

After the hemorrhage has been controlled the child should be warned not to blow his nose for some time.

inflammation of the trachea and bronchi may occur. The condition may occur acutely, but more often develops more slowly following a benign upper respiratory infection.

Authorities differ on the causative organism. In the case of an eight-year-old girl who developed a sudden virulent and fatal infection of this type, I was able to obtain a pure culture of *Bacillus influenzae* from the larynx at postmortem (Fig. 30). At various times hemolytic streptococci, pneumococci and other organisms have been reported as the etiologic agent.

The constitutional symptoms are usually severe, the voice is hoarse or often lost, and a rapidly developing *dyspnea* develops into a marked *stridor*, which at first is of an inspiratory nature due to the laryngeal obstruction, but later also develops into an expiratory stridor due to the obstruction of the trachea and bronchi by the tenacious secretion, and occasionally an actual membrane. The severe double stridor is accompanied by contraction at the suprasternal notch and in the epigastrium. At this stage the little patient appears desperately ill, has an anxious expression in the eyes, and looks toxic and tired, and the dyspnea and stridor are often accompanied by cyanosis or an ashy pallor. The following brief summary illustrates such a case.

A nine-month-old male infant contracted a cold which was followed by a croupy cough. On the fifth night of his illness he became restless early in the evening, the temperature rose to 104° F., and his mother noted that his respirations were becoming labored. She was alarmed by the contractions which she noted in the suprasternal notch. The child was taken to the hospital and upon reaching the admitting room the stridor had become so severe and cyanosis so marked that a Mosher tube was immediately inserted while preparation for tracheotomy was under way. Following tracheotomy, direct laryngoscopy revealed a severe glottic and subglottic edema. The convalescence was complicated by atelectasis of the right middle lobe (Fig. 31). Suction was employed frequently through the tracheotomy tube, and the fibropurulent mucous secretion was removed with great difficulty. After a stormy month's stay in the hospital, the patient made an uneventful recovery.

ACUTE LARYNGOTRACHEOBRONCHITIS

Acute laryngotracheobronchitis is a severe and often terrifying magnification of acute laryngitis. In this condition not only is the larynx acutely involved, but the trachea and



Fig. 30.—Larynx and trachea from a fatal case of laryngotracheobronchitis, showing the swollen epiglottis and subglottic tissues.

bronchi are also invaded by the inflammatory process. The submucosa, as well as the mucosa, is involved and a sticky, fibrinous exudate is produced; occasionally a membranous in-

tetany. Spasmodic croup is manifested by a typical *hoarse, barking cough*. Occasionally there seems to be a hereditary disposition to this condition. Usually the attack of croup is preceded by *hoarseness*, or an ordinary cold. The attacks of croup usually occur at night. The infant or child may have been perfectly well during the daytime and may emit an infrequent cough during sleep in the early part of the evening. Usually about midnight the child wakes with an attack of barking, paroxysmal cough. After a longer or shorter session of coughing, occasionally with some inspiratory *stridor*, the child will fall asleep again, and all will be well the following day except an occasional harsh cough and moderate hoarseness. The second and third nights are usually a repetition of the first night, following which the condition abates and the nightly disturbances occur no more.

Treatment

In the matter of treatment, cold, dry air seems to increase the spasmodic cough, while *warm, moist air* produces relaxation of the larynx and aids in overcoming the stridor and the harsh, barking cough. The use of *ipecac* in producing emesis is a time-honored remedy, but a good relaxing *sedative*, in which bromides are liberally combined with small doses of barbiturates, has proved considerably more effective and certainly less of a messy procedure. The infant or child should be confined to bed until the cold which is usually associated with the croup has entirely subsided.

ACUTE BRONCHITIS

Acute bronchitis is a frequent accompaniment of acute rhinopharyngitis. The cough in measles is probably the result of an acute bronchitis, and whooping cough is itself an inflammatory infectious disease of the bronchial tubes. The cough which accompanies acute bronchitis is at first likely to be dry and unproductive but later becomes looser in nature, producing mucous and mucopurulent *expectoration*. It is axiomatic that when an acute bronchitis does not clear up and show signs of improvement after four or five days, one should be highly suspicious of bronchopneumonia.

Fortunately, these severe cases are not commonly encountered, but are medical and surgical emergencies when they do occur. The severe subglottic edema renders intubation useless and *tracheotomy* in the severe cases is a life-sav-



Fig. 31.—X-ray of the chest from a tracheotomized infant suffering with laryngotracheobronchitis, showing atelectasis of right middle lobe due to occlusion of large bronchus by thick, tenacious secretion. Infant recovered after stormy course.

ing measure. The operation should not be postponed too long and aspiration of secretions following the operation may be necessary at frequent intervals. Opiates and atropine are contraindicated, and it is important that the room be kept at a considerable degree of humidity.

CATARRHAL LARYNGITIS (SPASMODIC CROUP)

Spasmodic croup usually occurs in the age incidence of from six months to three or four years and is of inflammatory origin. This condition should not be confused with other diseases in which spasm of the larynx occurs, as is manifested by the crowing, spasmodic contractions of the larynx in infantile

of crisis in lobar pneumonia, nor do we use the time-honored sponge for fever, and fresh air therapy, complicated chest binder or strapping for relief of pleurisy. Modern chemotherapy has done away with much of the agony and anxiety of the older treatment.

The mortality rate has taken a decided fall, and the morbidity rate for the secondary types of pneumonia in infants and children has declined considerably, owing to the new use of chemotherapy.

BRONCHOPNEUMONIA

Before the advent of chemotherapy, lobar pneumonia, the greatest incidence of which occurred in children from two to six years of age, was not so feared, nor was the prognosis so grave, as in the disseminated type, or bronchopneumonia, which was more common in infants under two years of age. The clinicians of the 1920's had evolved a very useful and instructive clinical classification for this disseminated type. One of the best of these classifications was proposed by Nassau, who divided bronchopneumonia in infants into the following types:

- | | |
|------------------------|----------------------------------|
| 1. Pulmonary form | 4. Intestinal or alimentary form |
| 2. Cardiovascular form | 5. Meningeal or eclamptic form |
| 3. Atonic form | 6. Toxic or septic form |

1. In the *pulmonary type* respiratory symptoms played the important role. Dyspnea and cough were the prominent symptoms in this type, and if sufficient areas of the lungs were consolidated, cyanosis also occurred. The infant was restless and wakeful, and the typical dilatation and contraction of the alae nasi, or rabbit-like breathing, was noted. In this type fatalities did not occur during the first days, and if the illness terminated in death, it was after a considerable duration. In general, it was felt that the prognosis in this type was comparatively favorable.

2. The *cardiovascular form* presented a distinct contrast to the pulmonary type. Cyanosis was an early symptom in these patients, accompanied by restlessness, anxiety and dyspnea. Very little pulmonary involvement was elicited on physical examination in these cases. They exhibited a small pulse, rapid cardiac action and low or sinking blood pressure. The skin

Capillary Bronchitis

In young infants the term "capillary bronchitis" has been used to designate a condition in which fine rales are heard scattered throughout the chest. No definite area of dulness may be elicited on percussion, and no certain consolidation may be demonstrated with the aid of the x-ray. Infants afflicted with this condition are usually rather ill, with considerable fever, dyspnea and sometimes cyanosis. I do not believe that a clinical differentiation between capillary bronchitis and a diffuse, finely disseminated broncho-pneumonia is possible. The term "capillary bronchitis" is generally applied when signs of consolidation cannot be demonstrated.

LOBAR PNEUMONIA

The literature contains many articles on the diagnosis and treatment of pneumonia in infants and children. The x-ray, with development of modern technic, has aided in the early diagnosis of pneumonia, and the great advances in chemotherapy came just subsequent to the laborious fruition of specific serum therapy for pneumonia. This last therapeutic measure was not too seriously attempted by those physicians especially interested in the treatment of young infants and children because of the difficulty of obtaining and typing properly the etiologic organisms.

Treatment

The latest advances in *chemotherapy* have vastly simplified the treatment of pneumonia in infants and children, because the latest sulfa-derivatives are more unselective, as far as the etiologic organism is concerned. The present-day intern in the modern hospital hardly uses his stethoscope or raises a callus on his plathismic finger in determining the extent or location of the consolidation. A quick fluoroscopic examination in the admitting room, or an emergency chest plate, will make the diagnosis, and the sulfa-derivative therapeutics which hardly an infant or child admitted with a temperature over 101° F. escapes, make the modern diagnosis and treatment a very simple, routine and rapid affair.

No longer do we count the odd days from the day of the inception of the disease on our fingers to determine the time

classification was often helpful in diagnosis and prognosis. It was, of course, valueless as far as therapy was concerned.

ASPIRATION PNEUMONIA

Occasionally pneumonia occurred in infants and children due to aspiration. The aspiration of infected *amniotic fluid* may produce antenatal and early neonatal pneumonia. If meconium be present in the aspirated fluid, an inflammatory reaction may develop in the lungs from this foreign material.

There are many substances which the infant of any age may aspirate which can produce pneumonia. When *dusting powders* containing zinc stearate were in vogue several decades ago, serious pneumonias from this source were not uncommonly seen. *Milk* may be aspirated by feeble infants and recently milk fat has been demonstrated as a cause of pneumonia in infancy. *Cereal foods, cod liver oil, mineral oil* and *foreign bodies* of nearly every variety have caused aspiration pneumonia. The *oily nose drops* are now taboo for the same reason.

The aspirated material, whether it be oil, powder or food, or whatever its nature, first acts as a mechanical irritating foreign body, after which infection is superimposed and pneumonia develops. Occasionally, following aspiration of a foreign body contaminated with the fungus of actinomycosis, a chronic pulmonary infection with this fungus may result. These infections are chronic and stubborn. Recently there have been reports from certain California valleys of coccidioid pulmonary infections which have afflicted infants and children of these areas. This has been termed coccidioidomycosis, and is frequently accompanied by erythema nodosum.

RHEUMATIC PNEUMONIA

In the past decade it has been recognized that a specific rheumatic pneumonia may occur in the same way as a rheumatic polyarthritis. Lesions in the lungs have been demonstrated to resemble pathologically the Aschoff bodies in other tissues. In virulent cases of rheumatic fever with associated rheumatic heart disease an associated rheumatic pneumonia may often be demonstrated.

color varied from cyanosis to pallor or sickly grayish hue. Often the superficial veins of the chest and abdomen were prominent and seemed dilated. Patients suffering with this type of the disease were liable to sudden collapse and sudden exitus. The vasomotor centers and the heart were severely affected in this type and gave rise to the cardiac and vascular failure.

3. The *atonic form* was characterized by extreme loss of tone in the skeletal muscles. The infant lay limp in his crib and moved but little. The arms and legs were flaccid, as though paralyzed. Marked asthenia, stupor and muscular relaxation characterized this clinical type.

4. The *alimentary form* was ushered in by vomiting, diarrhea and the loss of weight. A considerable time elapsed before the pulmonary involvement was suspected or detected. The weight loss was usually considerable and a moderate to marked tympany developed and as the alimentary symptoms were treated and relieved, pulmonary involvement became evident.

5. In the *meningeal or eclamptic type* of the disease such symptoms as rigidity of the neck and extremities, opisthotonos, convulsive movements of the eyes and mouth and generalized convulsions occurred. These symptoms all suggested an early meningitis. These patients were usually stuporous or unconscious, and this condition usually lasted for a number of days. Consciousness returned several days before the defervescence of the fever. The meningeal form was characterized by recurring convulsions.

6. The *toxic form* was manifested by an acute fulminating onset which in a few hours changed an apparently healthy infant into an extremely ill one, on the verge of collapse. Usually in this type the fever was high and the cyanosis marked. The course was rapid and often fatal within 48 hours of onset. It was assumed that these pneumonias were of haematogenous origin and the accompanying septicemia caused the rapid and often fatal course.

The above classification was made entirely on a clinical basis and had nothing to do with etiology. There were often mixed forms of these various types of pneumonia. Such a

DELETERIOUS EFFECTS OF LIPIODOL AND ALCOHOL INJECTIONS ON THE TISSUES OF THE CENTRAL NERVOUS SYSTEM

A. VERBRUGHEN, M.B. CH.M. M.S. F.A.C.S.*

It has been suggested that I devote a little time to a consideration of the ill effects of lipiodol and alcohol when injected into the subarachnoid space. If the discussion is limited strictly to the ill effects produced by these substances, a very one-sided view is obtained, but, if it is reasonable to include some of the main indications and advantages, then the subject should be well worth while. An unrestricted indictment would cause the practitioner to be extremely hesitant in allowing the use of these substances, even when they are indicated.

At the outset it is only fair to state that both alcohol and lipiodol have a very definite place in the armamentaria of those interested in the diagnosis and treatment of disorders of the nervous system. It is also proper to say that both procedures have been abused by those unfamiliar with their proper indications and use. Some men are inclined to push a simple method beyond the boundaries of its proper use, which leads to bad results. I have used these two substances sparingly and with a wholesome respect for the damage they can do. This may account for the fact that only minor setbacks have been observed. It is possible that I have been too conservative and that I have failed to use the procedures to their fullest advantage, but a perusal of the articles of those who introduced these substances shows that they were well aware of necessary restrictions.

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Adverse Experiences with Lipiodol

I wish to report four cases in which lipiodol produced rather minor ill effects following its injection. Although it is possible that one or two cases with deleterious effects may have been overlooked, it is unlikely because I have consulted not only the files but the memories of members of the staffs of the hospitals where these procedures were carried out. The doctor who refers a patient to you is very likely to remember any harm that comes to the patient. Further, these patients have all been completely in my care from start to finish, and the reports represent a very personal experience.

In two instances there was a mild febrile reaction which was thought to be due to the lipiodol. In one case there was a more marked febrile reaction with what might be described as a meningismus, there being a positive Kernig sign, a positive Lasègue sign and a stiff neck. This subsided in thirty-six to forty-eight hours.

CASE I.—Miss V. J. was admitted to the Presbyterian Hospital on February 19, 1938. She was a very high-strung woman thirty-one years of age. About seven months previously she had received an injury to her back while swimming. Since then there had been a constant dull pain in her back at about the level of the third lumbar vertebra. This pain was aggravated by movement of any kind, so that getting about and walking were uncomfortable. The pain was also aggravated by coughing and sneezing.

Neurological examination was negative. The third lumbar spine was very tender to the touch. Flat plates of the lumbar spine were negative and so were the examinations of the pelvis and the stools and x-ray studies of the gallbladder, chest, stomach and colon. An orthopedist did not cast suspicion on the sacro-iliac joints.

Five cubic centimeters of lipiodol were injected into the lumbar canal with the expectation that a herniated nucleus pulposus would be demonstrated. The fluoroscopic examination of the subarachnoid space did not demonstrate a lesion. The patient, however, reacted adversely to the lipiodol. Sixteen hours after the injection, she complained of pain down the backs of both legs; her neck was stiff and there was a positive Kernig as well as a Brudzinski sign. Twenty-seven hours after the injection

SUBARACHNOID LIPIODOL INJECTIONS

Lipiodol is a chemical compound of poppy-seed oil with about 40 per cent iodine. The solution is rather irritating and should be used with caution. It is not as generally useful as is commonly supposed by the uninitiated, who seem to believe that it is the complete answer to the problem of establishing the level of cord compression. As a matter of fact, until the limelight shone on the syndrome of the herniated nucleus pulposus, it had a very limited use in hospitals staffed with good neurologists. It is an axiom that the better the neurological examination, the less the need for contrast media. This applies equally well to the use of air for the diagnosis of cerebral lesions.

Indications for Use

The principal use of lipiodol is to establish the level of cord compression in those cases in which there is a *partial spinal block*. In patients with a *herniated nucleus pulposus* it establishes the level of the projection into the spinal canal, though recent articles by Spurling and Bradford¹ have shown that here again the neurological picture is usually sufficient to localize the lesion. In cases of "slipped disk" in which the x-ray picture is positive, the lipiodol can be removed at operation a few hours later, thus limiting its chances of causing irritation. Because of its irritating effects, it should not be used when an inflammatory lesion is suspected.

Irritating Effects

Lipiodol is radiopaque and is heavier than spinal fluid. When it is not removed at operation, it is allowed to gravitate to the lower end of the spinal canal, where it comes in contact with the cauda equina and especially the lower roots. Its principal irritative effects are felt at this point with resulting *pains in the legs*, especially along the course of the sciatic nerves. The pain may last from a few hours to ten days or more. Pain is the only symptom and there have not been any signs except those associated with pain, such as a Lasègue sign.

the patient had fallen from a horse, landing on the buttocks. For two or three years there had been recurring attacks of pain in the back until 1938 when the pain had radiated down the back of the left leg. The pain had become much worse in the last four months and was aggravated by coughing and sneezing.

Neurological examination was negative except for some hypaesthesia on the outer part of the left thigh extending up to the buttock. The spinal fluid examination was negative, the total protein being 45 mg. per 100 cc. Barium examination of the colon and fluoroscopic examination of the chest were negative. X-ray plates of the lower lumbar spine revealed thickening of the margins of the left sacro-iliac joint. A gynecologic consultant felt two small masses about the size of beans in the cul-de-sac and suggested that these were endometriosis. This idea was somewhat substantiated by the fact that the sciatic and back pains were worse just before and at the beginning of the menstrual period. The usual laboratory examinations of the urine and blood were negative, as was the general physical examination. The patient had not borne children.

Accordingly, 5 cc. of lipiodol was injected into the spinal canal. No abnormality of the canal could be demonstrated. That night the patient complained bitterly of pain in the back. The next day she was nauseated and vomited. At noon, about thirty-six hours after the injection, she felt at her worst with nausea and pain in the back. The temperature was 100° F. by mouth. The fever rapidly subsided and she was discharged the next day. The pain in the back with aggravation of the sciatic pain continued for fourteen days.

The patient still has bouts of sciatic pain and her symptoms have continued to progress up to the present time (September, 1940). The lipiodol was re-examined under the fluoroscope, but no abnormality could be found. The patient went elsewhere for a thorough neurological examination and for fluoroscopic study of the lipiodol, but still no abnormalities were demonstrated in the spinal canal. The fascic line has been cut on the left side, with a little relief.

Here again there was a negative lipiodol examination in a symptomatic individual with an adverse reaction which was partly objective but mostly subjective.

A fourth patient who showed a rather severe reaction was of interest because of his final status. This is a type of case

the highest temperature of 101.2° F. was recorded by mouth. This was accompanied by a chill. The next day, about forty-eight hours after the lipiodol was injected, the temperature was normal and all the signs and most of the symptoms were relieved. The patient still complained of vague discomfort in the back of the legs and this continued for about ten days and then entirely disappeared.

This is probably the worst reaction to lipiodol which has occurred in my experience. It was accompanied by very definite signs of meningeal irritation as well as an irritation of the roots of the cauda equina. In the following case the patient did not have much febrile reaction but the general aspects closely simulate those of the case just mentioned.

CASE II.—Mr. A. F., thirty-three years of age, was admitted to the Presbyterian Hospital in April, 1935, complaining of an encircling pain radiating from the back and the abdomen just above the umbilicus. The pain was more severe on the right side, with paresthesia of the right thigh. The pain had been present since an accident in 1931 in which his back was hurt, though apparently no damage was done to the spinal cord. For five or six days the back had been very painful and he was put in a cast for five months.

General and neurological examinations were negative. On April 13, 5 cc. of lipiodol was injected into the lumbar subarachnoid space and a fluoroscopic examination was made. No abnormality in the outline of the spinal canal was seen. The following morning the patient complained of headache and pain in the lower end of the spine. By 4 P.M. his temperature was 102° F. and the headache was severe, requiring sedatives. There were no neurological signs. The next morning the temperature was 100° F. and fell to normal that evening.

The patient was discharged on April 16. He was seen again on April 20 complaining of pain down the back of both legs which had become severe the day following his discharge from the hospital. These pains continued in spite of sedatives for about three weeks and then gradually subsided.

CASE III.—Mrs. C. B., thirty-eight years of age, was admitted to the Presbyterian Hospital in April, 1939, for a lipiodol injection to rule out herniated nucleus pulposus. In November, 1935,

the patient had fallen from a horse, landing on the buttocks. For two or three years there had been recurring attacks of pain in the back until 1938 when the pain had radiated down the back of the left leg. The pain had become much worse in the last four months and was aggravated by coughing and sneezing.

Neurological examination was negative except for some hypalgesia on the outer part of the left thigh extending up to the buttock. The spinal fluid examination was negative, the total protein being 45 mg. per 100 cc. Barium examination of the colon and fluoroscopic examination of the chest were negative. X-ray plates of the lower lumbar spine revealed thickening of the margins of the left sacro-iliac joint. A gynecologic consultant felt two small masses about the size of beans in the cul-de-sac and suggested that these were endometriosis. This idea was somewhat substantiated by the fact that the sciatic and back pains were worse just before and at the beginning of the menstrual period. The usual laboratory examinations of the urine and blood were negative, as was the general physical examination. The patient had not borne children.

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Here again there was a negative lipiodol examination in a high-strung individual, with an adverse reaction which was partly objective but mostly subjective.

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that has been a source of great annoyance to insurance companies and for which the industrial commissions have had to hold many hearings.

CASE IV.—Mr. J. H., thirty-five years of age, was admitted to the Presbyterian Hospital on August 7, 1938. In November, 1937, the patient fell on the ice and hurt his back. For several days the back was sore and stiff, making him unable to stoop or to lift things. In March, 1938, pain was felt which radiated down the back of the left leg from the hip to the ankle. In June attempts were made to relieve him by "injecting" the sciatic nerve. He was also given intramuscular injections of milk. None of these measures gave relief.

Neurological examination on admission demonstrated a marked left Lasègue sign, a slight crossed sign as well as a slight right Lasègue sign. All the deep reflexes were lively. There was some wasting of the left thigh where the circumference was 1.5 cm. less than the right. A small, rather indefinite patch of hypalgesia was demonstrated on the outer part of the left leg above the lateral malleolus. The pain was of typical sciatic distribution and was aggravated by coughing and sneezing. The flat plates of the spine were negative.

Under these circumstances a diagnosis was made of herniated nucleus pulposus between the fourth and fifth lumbar vertebrae. Lipiodol was injected into the lumbar spine at noon on August 8. During the fluoroscopic examination the patient complained of excruciating pain in the left leg each time the lipiodol was made to pass the third lumbar vertebra on the left side. This was observed by the neurological team and the radiologist. No deformity of the spinal canal could be demonstrated.

The patient complained of pain in the back that night and he voided early next morning (August 9). During the day he complained bitterly of pain in both legs, worse in the left, and over the coccyx. He was given codeine and aspirin without much relief. That night the patient felt nauseated, and his temperature had risen to 101.6° F. by mouth. The admission temperature had been 100° F. During the night and the next day (August 10) the patient was in severe pain, requiring morphine in quarter grain doses to control it. He was unable to void during this time. His temperature returned to normal in four days and on August 12 he voided normally. An epidural injection was made with little effect and he was discharged from the hospital.

The patient returned one month later for further observation, at which time he stated that the exaggerated pain in his legs had continued for ten days after his discharge from the hospital. He became dissatisfied and went elsewhere for the laminectomy we advised. A protruded disk was found and removed and the patient was seen by me ten weeks later. His wound was draining and he had developed a sciatic syndrome on the opposite side. He was immediately sent back to the surgeon who had operated upon him.*

These cases represent my adverse experiences with lipiodol, and after giving them due consideration there does not seem to be much cause for alarm. The substance was used in many other cases, especially those in which a slipped disk was suspected, but in most of these the injection was followed within two or three hours by operation, at which time some of the lipiodol was removed.

Meningeal Reactions to the Presence of Lipiodol.—Even when the lipiodol is said to have been completely removed, traces or even large quantities are subsequently demonstrated in the subarachnoid space. Garland and Morrissey¹ have recently reviewed the literature and studied cases in which lipiodol had previously been injected. In some of these the oil was said to have been removed but they found several cases in which the lipiodol was visualized at a later date in the cranial cavity. They came to the conclusion that it causes little damage to the brain. In reviewing my experience there seems to be little reason for serious objection on this score to the use of lipiodol. The meninges are sure to react to some extent to any foreign substance in contact with them. Walsh and Love² investigated this meningeal response in twenty-four cases; nearly all the cases showed an increase in the cell count of the spinal fluid to 20 or 30 cells per cubic millimeter. The

* Since writing the clinic, I have seen a case in which the injection of lipiodol resulted in a very severe meningeal reaction with a high fever, stiff neck, coma, a very high cell count and cloudy fluid, and ultimately in death. Although in this instance the lipiodol was injected inadvisedly in a subacute inflammatory disease, the attending physician had felt that it represented the only possible means of finding out whether a surgical condition was present. As the man was failing rapidly, it may, in some ways, have been justified.

protein in the spinal fluid was also raised. The greatest reaction was 550 polymorphonuclear neutrophils to the cubic millimeter of fluid on the second day. Most of the cases studied were of herniated nucleus pulposus.

Favorable Experience with Lipiodol

The following case report represents, to my mind, the proper use of lipiodol:

CASE V.—Mrs. R. D., forty-nine years of age, was admitted to the Presbyterian Hospital on January 20, 1933, complaining of

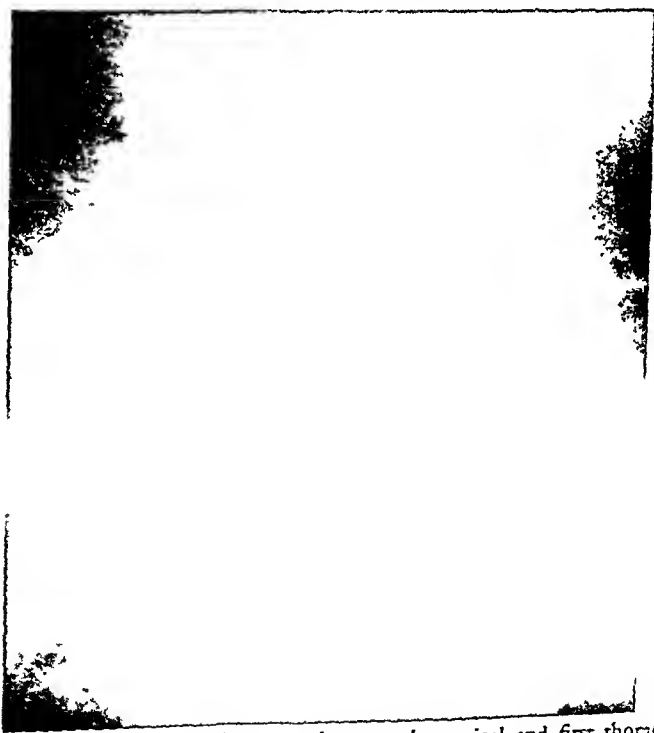


Fig. 32.—Lipiodol arrested between the seventh cervical and first thoracic vertebrae (patient in the upright position).

inability to walk and loss of sensation in the legs. The peculiarities of sensation had been present for a year and a half and the gradually progressive difficulty in walking for eight months.

On admission the patient was barely able to stand at the bedside. The deep reflexes were exaggerated in the legs; there was cable clonus and bilateral extensor plantar response (Babinski's sign). A sensory level was found at the second thoracic segment, but owing to a language difficulty on the part of the patient, this level as ascertained from her was not regarded as being sufficiently trustworthy. Spinal puncture revealed an almost complete spinal block and a total protein of 250 mg. per 100 cc. of fluid. The Wassermann reaction was negative in the spinal fluid, although when taken elsewhere in 1933 it was said to be positive.

A diagnosis was made of intradural, extramedullary spinal cord tumor about the first thoracic segment. Because of the language difficulty in the subjective examination for level, it was agreed upon consultation that it was proper to use lipiodol. On January 24, 5 cc. of lipiodol was injected into the cisterna magna. Under the fluoroscope the lipiodol was seen to stop at the seventh cervical vertebra, with a prong extending from each side to the first thoracic vertebra (Fig. 32). There was some reaction, as was expected, to the lipiodol arrested in the neck. For two days there was a temperature up to 100° F. On January 26 laminectomy was carried out and a meningioma about the size of a large olive was removed from under the first thoracic lamina. The patient made a steady and uneventful recovery and when last seen in 1936 was doing her own housework and appeared normal in every way. The tumor was found at the point indicated by neurological examination and lipiodol might have been omitted, had we felt that the sensory level as ascertained from the patient was trustworthy.

Limitations of the Lipiodol Examination

As in any other method of investigation, the limitations of lipiodol examination must be understood in order to use it to advantage, its simplicity has been the cause of its abuse in incompetent hands. I understand that industrial commissions view lipiodol with particular disfavor because of what they regard as the objectionable sequelae of its use. Lipiodol found in the spinal canal by means of x-ray pictures, even several months after its diagnostic use, is credited with being the cause of vague and diffuse pains in the legs and back. This seems to be accepted in the absence of objective neurological signs, although the patient presents himself to receive

as much compensation as possible. Many patients who present themselves before commissions complain vehemently of headache, dizziness and backache which is said to be due to the presence of lipiodol in the canal. It is a matter of fact, however, that these often follow spinal puncture and would probably be better attributed to the puncture. Puncture headaches are immediately relieved by lying down. In any case it is extremely difficult to evaluate the subjective phenomena in the individual seeking compensation. These long-drawn-out vociferous complaints are very rarely heard from evil-doers or those with no possible chance of gain.

Summary and Conclusions

To summarize, then, lipiodol should be used *sparingly* and *only in cases in which a proper conclusion cannot be reached without it*. It can never replace a thorough neurological examination. It will be found most useful in cases with a partial spinal block in which a sensory or motor level is hard to establish, or in cases in which no block exists. Its use in instances of suspected herniated nucleus pulposus with a typical example of a proper indication; however, the syndrome is now better understood and lipiodol is no longer so important in its diagnosis. Lipiodol should not be used if there is any evidence of inflammatory disease in the subarachnoid space.

The substance should be warmed to body temperature before it is used and it can then be injected into the cisterna magna or into the lumbar canal. Arrangements should be made to carry out any necessary operative procedure immediately after the injection, when as much of the lipiodol as possible should be removed from the subarachnoid space. Bearing these points in mind I have found that the use of lipiodol in the subarachnoid space is, by and large, beneficial to the patient.

ALCOHOL INJECTIONS FOR THE RELIEF OF INTRACTABLE PAIN

Alcohol when injected into the subarachnoid space produces a reaction from the meninges and has a sclerosing effect on the nervous tissue with which it comes in contact. The

principle of its use here is similar to that in blocking other sensory nerves, namely to prevent temporarily the conduction of painful impulses. Alcohol has long been used in the injection treatment of trigeminal neuralgia. Harris, when injecting the gasserian (semilunar) ganglion through the foramen ovale, reported untoward results when the substance accidentally spilled into the subarachnoid space.

Dogliotti in 1931 introduced the method of subarachnoid alcohol injection into the spinal canal for the relief of intractable pain. Here again we were provided with a very simple technic which really only required a spinal puncture needle and some alcohol, with the result that the method was used indiscriminately and by those unfamiliar with the anatomy of the nervous system and unaware of the risks involved through introducing a destructive substance close to delicate nervous tissue. There were even untoward results reported by those who were perfectly familiar with its proper use.

Deleterious Effects

The most common undesirable disturbance following alcohol injection into the subarachnoid space is *motor weakness* and *bladder disturbance*. In a fairly active clinic devoted to the problem of pain at Cook County Hospital, alcohol is used quite frequently and no untoward results have been noticed. The procedure is part of the armamentarium of all those who have to deal with pain and it must be employed rather frequently. I used the method sparingly and perhaps not to its utmost advantage, but at least I am spared the disappointment of causing further trouble to the patient in pain. The bad effects that I mention to you are relayed from the literature and from occasional studies made of patients in consultation.

As far as I know, no animal experiments have been conducted measuring the amount of nervous damage that alcohol does in the subarachnoid space. Alpers found degenerative changes in the cords of patients who had alcohol injected, though no neurological signs were elicited during life.

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fects of this procedure. Most of the trouble is caused by the *improper position* of the patient and the use of *too much alcohol*. Groff has produced an excellent article describing the proper technic to be employed. The complications are described under the following headings: (1) *Headache, nausea and vomiting* due to ascent of the alcohol. I believe that some of these symptoms are occasioned by making the spinal puncture in persons who are in severe pain and who may already be emaciated and weak. (2) *Motor weakness* due to improper position of the patient and the use of too large a quantity of alcohol. Groff believes that 9 mm. is the maximum amount of absolute alcohol which can safely be used in the subarachnoid space. (3) *Incontinence of urine and feces* from the use of too much alcohol too high up, *i.e.*, in the region of the second and third lumbar vertebrae. (4) In one case in which alcohol was injected into the first thoracic vertebra, a transverse *myelitis* resulted. Groff quotes Alpers as saying that the injection should never be done above the first lumbar vertebra.

I have never injected alcohol above the second lumbar vertebra and I have never injected more than 1 cc. of absolute alcohol at a time. Much attention is given to the position of the patient. Perhaps there has been some undue timidity on my part but at least the method has not suffered. The results have been satisfactory to good in about 50 per cent of cases, and no deleterious effects have been observed, except in one instance.

Illustrative Cases

CASE VI.—An elderly woman was admitted to the Presbyterian Hospital in the spring of 1934 with intractable pain in the legs due to a metastatic growth in the spine from a carcinoma of the breast removed at operation two years before.

The patient was given three injections, each of 1 cc. of absolute alcohol in four days, in an attempt to relieve the pain. The first injection had relieved the pain in the left leg but two injections were required to relieve the pain in the right. The day following the third injection the patient became very active and disoriented and acted in many ways like one suffering with alcoholic delirium tremens. This condition lasted for several days.

When, later, she became coherent, it was learned that her legs were free from pain. The medical attendant, the neurological consultant and I all felt that the sudden change in the patient was in some way connected with the injection of the alcohol into the subarachnoid space.

Although the case I am about to report can scarcely be described as an untoward result from the injection of alcohol, I mention it to draw attention to the fact that a pain may be so severe that almost any procedure is justified. I described this case in a recent article on intractable pain but since then there have been further developments.

CASE VII.—Mr. G. K., thirty-nine years of age, was admitted to the Presbyterian Hospital in October, 1939, complaining of constant knifelike pain in the perineum. In February, 1939, a bladder tumor, as well as his left kidney, had been removed. In August, 1939, a further operation was performed on the bladder tumor, which was said to be papilloma. The pain in the perineum had been present for a month before the second operation. In September, 1939, the patient was having severe pain in the perineum, and as his bowels did not move properly and because of the pain, his abdomen was opened and adhesions between the bowel and bladder were reported to have been removed. The pain in the perineum was not abated. An epidural injection did not relieve him.

On October 14 an epidural injection was given by me with instant relief. A few days later, with the patient in suitable position, 1 cc. of absolute alcohol was injected between the fourth and fifth lumbar vertebrae. This was done very slowly. At first there was a burning sensation in the perineum which disappeared in about a half an hour. However, the patient immediately began to experience more difficulty in emptying his bladder than he had before the injection. Next day an indwelling catheter was inserted. Six weeks after the injection he was beginning to void without the catheter. The pain disappeared with the injection. Soon the function of the bladder will return and so will the pain.

This is the case report as it appears in another paper. The patient returned at the beginning of May, 1940, complaining of the old perineal pain. The function of the bladder was fairly good. On May 5, 1940, a bilateral cordotomy was done

fects of this procedure. Most of the trouble is caused by the *improper position* of the patient and the use of *too much alcohol*. Groff has produced an excellent article describing the proper technic to be employed. The complications are described under the following headings: (1) *Headache, nausea and vomiting* due to ascent of the alcohol. I believe that some of these symptoms are occasioned by making the spinal puncture in persons who are in severe pain and who may already be emaciated and weak. (2) *Motor weakness* due to improper position of the patient and the use of too large a quantity of alcohol. Groff believes that 9 mm. is the maximum amount of absolute alcohol which can safely be used in the subarachnoid space. (3) *Incontinence of urine and feces* from the use of too much alcohol too high up, *i.e.*, in the region of the second and third lumbar vertebrae. (4) In one case in which alcohol was injected into the first thoracic vertebra, a transverse *myelitis* resulted. Groff quotes Alpers as saying that the injection should never be done above the first lumbar vertebra.

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COARCTATION OF THE AORTA

A Presentation of Two Symptomless Patients

ITALO F. VOLINI, M.D., F.A.C.P.*

and

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In these days of medicine when the sphygmomanometer plays such an essential part in the physical examination, readings on the instrument of a high value too often are used to diagnose a disease rather than to determine a physical finding. We frequently fall into the error of evaluating the high reading immediately as the disease, essential hypertension, of the benign or malignant variety. The routine office or clinic study of the patient otherwise will show no marked abnormal deviation, so that "benign essential hypertension" becomes the diagnosis. An occasional review of the many various causes of the symptom, hypertension, can well be of value, as the following case illustrates.

CASE 1

History.—J. H., a white youth aged seventeen years, was referred to us after several examiners had discovered hypertension, with a diagnosis of high blood pressure or essential hypertension. His sister, a nurse, requested that something be done for this pressure elevation. He has no particular complaints, except that he notices some slight dyspnea on violent exertion, appreciable for the past six or seven years. He is working as a clerk during the summer vacation, and attending high school during the school year. Measles at three years of age, diphtheria at four and a tonsillectomy at eight constitute the only significant past com-

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at the third thoracic segment, with complete relief of pain until the patient died, the victim of extensive malignant disease, two months later.

Advantages

Although a good deal has been said about the destructive effect of alcohol, we must weigh the advantages against the disadvantages. There is a group of neurologists and neurosurgeons who throw up their hands in horror at the idea of letting alcohol roam about near delicate nervous tissue. Nevertheless, a patient in severe pain must obtain relief, quickly and with as little risk as possible. Neither can one be too squeamish about giving relief to patients whose life expectancy is very short. It is probably better to end one's days in comparative comfort and in full control of one's mental faculties, even if one has some motor weakness and perhaps an indwelling catheter. The alternatives are cordotomy with its operative risk or many continued and inadequate injections of morphine with the accompanying apprehensive attitude and the blurred mentality.

CONCLUSION

Mention has been made of the deleterious effects of lipiodol and alcohol when injected into the subarachnoid space. Because the procedures are within the technical scope of all medical practitioners, there is all the more reason to emphasize the dangers and drawbacks, as well as the necessity for a clear understanding of the proper technic.

BIBLIOGRAPHY

1. Garland, L. Henry and Morrissey, Edmund, J. Iodized Oil Collections after Lumbar Myelography. *Surg., Gynec. & Obst.*, 70: 196, 1940
2. Groff, R. A.: Alcoholic Injection for the Relief of Intractable Pain *Surg. Clin. N. Am.*, 19: 1569 (Dec.) 1939.
3. Walsh, M. N. and Love, J. G.: Meningeal Response Following the Subarachnoid Injection of Iodized Oil. *Proc. Staff Meet., Mayo Clin.*, 13: 792, 1938.
4. Spurling, R. Glen and Bradford, F. Keith: Neurologic Aspects of Herniated Nucleus Pulposus. *J.A.M.A.*, 113: 2019 (Dec.) 1939.

side at the lower margin of the eighth and ninth ribs, just below the angle of the scapula, *prominent pulsating vessels are noticed*, throbbing and pushing out the skin with each pulsation. They are noticeable for a distance of about 2 cm. Likewise, in the interscapular area on both sides on a level with the transverse spine of the scapulae we see pulsating vessels which course diagonally downward for about 5 cm., disappearing underneath the scapulae.

Of course, immediately, the diagnosis is thus suggested and blood pressure determinations made on the right arm show a



Fig. 34 (Case I).—Chest film. Very pronounced rib excavations are noticeable. The aortic knob is absent.

level of 196 mm. of mercury systolic and 100 diastolic. The femoral pulse is barely appreciable, but no blood pressure reading can be obtained on either lower extremity. The dorsalis pedis pulse cannot be obtained on either foot.

X-ray Examination.—This interesting case of coarctation of the aorta demands further investigation. Temperature readings in the mouth are normal. The 6-foot film of the chest reveals the heart with slight enlargement to the left and extensive scalloping of the lower margins of the third to the ninth ribs inclusive (Fig. 34). The scalloping is very marked particularly on the left side,

plaints. There has been no history of rheumatic infection, growing pains, chorea or severe attacks of tonsillitis. The patient is of more than average intelligence, has an excellent body build and is very active physically.

Physical Examination.—The physical examination reveals a blood pressure reading of 190 mm. of mercury systolic and 100

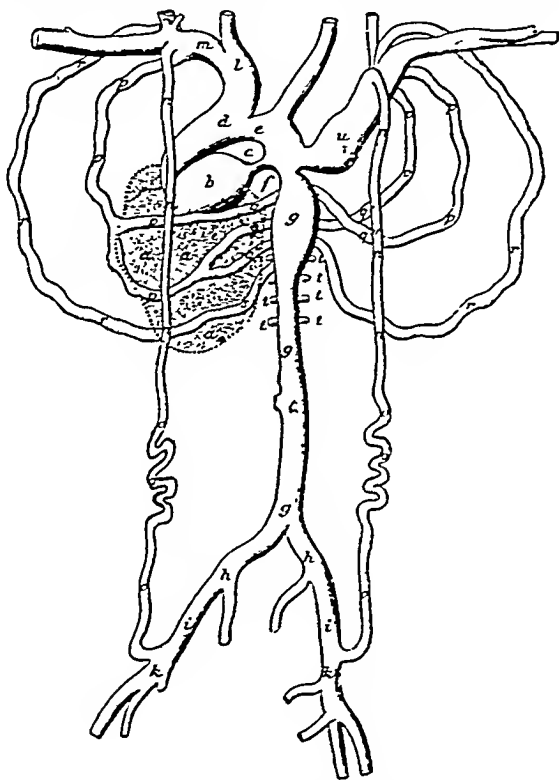


Fig. 33.—Diagram illustrating coarctation of the aorta and the common anastomoses. Reynaud's patient who died at ninety-two years of age. (A. Reynaud, "Observation d'une oblitération presque complète de l'aorte, etc." J. hebdomadaire de médecine, 1828, I: 161.)

diastolic. The heart is slightly enlarged to the left, measuring 10 cm. to the left of the midsternal line with the apex in the fifth intercostal space. There is a loud systolic murmur at the apex. A systolic murmur is audible over the aortic cartilage and is transmitted into the carotids. When we examine the back on the left

T in Lead I. In fact, T_1 and T_2 are equal to the respective R waves. Further study shows normal circulation time by decholin, normal venous pressure and normal vital capacity.

Discussion

This patient demonstrates most of the classical evidence encountered in the constriction or obliteration of the descending arch of the aorta at the point of insertion of the normally obliterated ductus arteriosus. There results, as seen in this individual, the extensive *collateral circulation* between the posterior scapular, interscapular and subscapular arteries, in addition to the superior intercostal branch of the subclavian artery (all of which receive blood from the aorta above the site of constriction, and deliver it to the aortic intercostals which pour this blood into the aorta below the coarctation).

As in this patient, the collateral circulation frequently gives rise to an *increase in size* of the collateralized vessels, owing to the abnormal amount and pressure of the blood which these vessels carry. Consequently, where they contact bone such as the inferior rib margins and vessel angulation points, *erosion of the bone* results which is so beautifully illustrated in the roentgenogram of the chest.

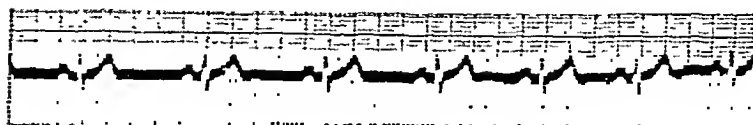
The major collateral circulation in this patient thus appears to be by way of the intercostal arteries, thus accounting for the magnitude of the changes in the ribs. Stress must be laid on the fact that the physical examination reveals the diagnosis.

CASE II

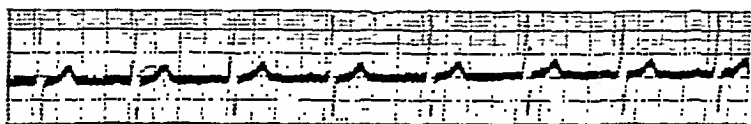
History.—The patient, a white man eighteen years of age, was referred to us by his physician because of hypertension. He complains of precordial pain. He has been found to have a blood pressure of 198 mm. of mercury systolic and 60 diastolic, and a diagnosis of rheumatic heart disease with mitral and aortic valvulitis has been suggested. The history reveals several attacks of severe tonsillitis for which tonsillectomy was performed at eight years of age. He is above the average in mental and intellectual development, having finished high school and now being occupied in defense work on an eleven or twelve hour daily schedule, often working seven days a week.

Physical Examination.—The blood pressure on the right arm

especially the eighth and ninth ribs, where the pulsating intercostals were noted on the physical examination. This excavation of bone is not accompanied by thickening or new bone formation. In the flat plate there is an absence of the aortic knob.



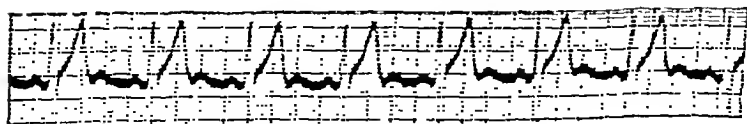
Lead 1.—Between right and left arms.



Lead 2.—Between right and left leg.



Lead 3.—Between left arm and left leg.



Lead 4.

Fig. 35 (Case I).—Electrocardiogram.

In the left oblique film the aortic arch is poorly visualized and terminates very abruptly at the isthmus. The retro-aortic and retrocardiac spaces are clear.

Electrocardiography.—The electrocardiographic tracing (Fig. 35) reveals the tendency to right axis deviation with a prominent



Fig. 37 (Case II).—Oblique film (right) showing clear retro-aortic space.



Fig. 38 (Case II).—Oblique film (left) showing clear retrocardiac space.

is 198 mm. of mercury systolic and 60 diastolic, with a sound audible below this diastolic level, which disappears when the reading is down to 10 mm. of mercury. The left arm reading is 190 systolic and 8 diastolic, with the diastolic sound disappearing at 40 mm. of mercury. The radial pulse is of the typical aortic regurgitation type. The carotids, however, do not throb violently. The apex beat is forcible in the sixth intercostal space 12 cm. to the left of the midsternal line. Upon palpating the heart apex, the lower edge of the hand feels a thrill or bruit which was not palpable at the apex. On moving the hand down-

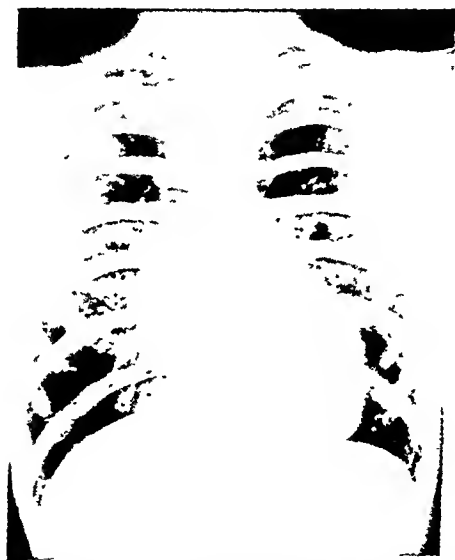


Fig. 36 (Case II).—Chest film showing cardiac enlargement, rib excavations, absence of aortic knob and straight left border of aortic shadow.

ward just below the thoracic insertion of the left rectus, a small mass is palpable where this bruit arises—a cirroid aneurysmal dilatation. With the stethoscope, the murmur audible here can be traced downward along the left rectus abdominis muscle for about 5 cm.

Upon auscultation of the heart itself, systolic and diastolic murmurs are audible at the apex as well as at the aortic cartilage and the carotid vessels in the neck.

The femoral vessels, the popliteals, and the dorsalis pedis vessels show no pulsation. Upon examination of the back, in the

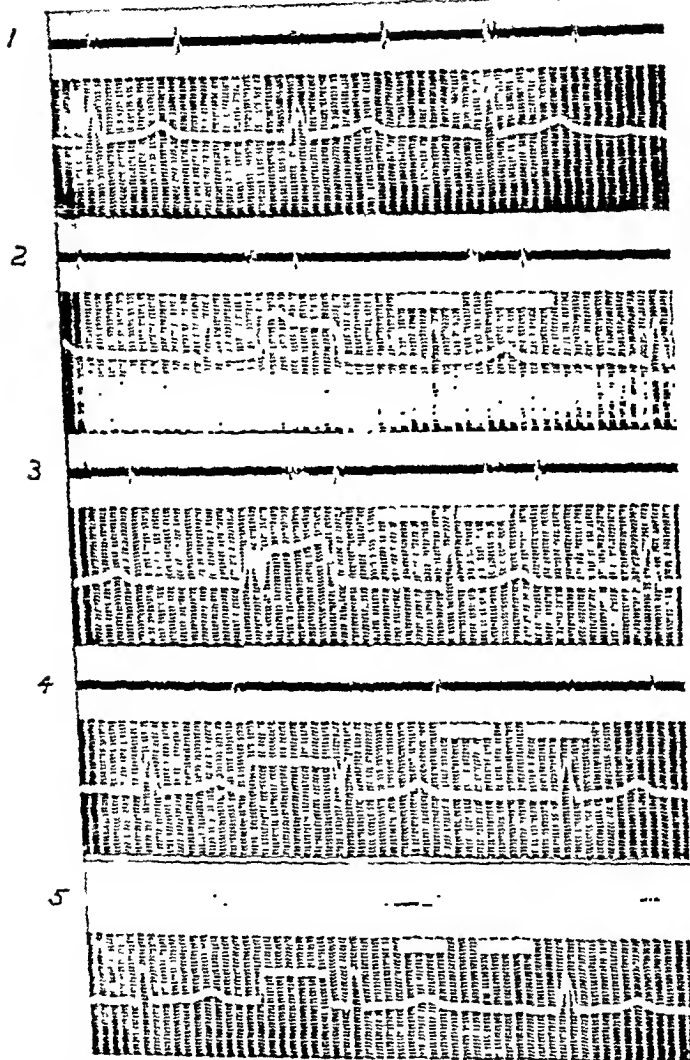


Fig. 40 (Case II).—Stethographic registrations of the various locations described in the text. The numbers show the sound track lines with the double-speed electrocardiogram of Lead 2 below for the purpose of timing the murmurs.

interscapular areas on both sides at the level of the transverse spines of the scapulae, large, obliquely coursing arteries are found which pulsate vigorously.

X-ray Examination.—The chest film (Fig. 36) shows the heart to have a markedly increased transverse diameter, giving the appearance of a combination of an aortic and mitral valve lesion. The aortic knob is absent. The oblique films (Figs. 37 and 38), left and right, show an absence of the descending thoracic aortic

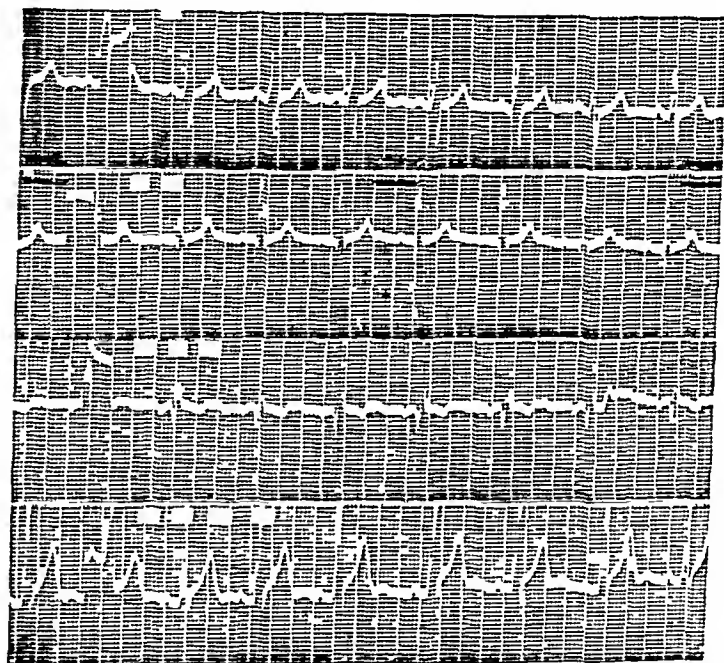


Fig. 39 (Case II).—Electrocardiogram.

shadow with a very short aortic arch. Upon close inspection, scalloping of the inferior rib margins again is seen, although the scalloping is not nearly so evident as in the first patient. The electrocardiographic tracing (Fig. 39) again shows the tendency to right axis deviation, with T greater than R in Lead 3.

Oscillometry.—The oscillometer is placed upon the right and left arms, with readings of 7 and 6 respectively. Blood pressure readings on the legs are unsuccessful. The oscillometer shows maximum deflections of 3 on the thighs and 2 on the calves and,

tion of the aorta with aortic regurgitation. The insufficiency was accompanied by a bicuspid aortic valve. This probably is present in our second patient.

Evidence regarding the collateral circulation, obtained on physical and x-ray examination, points to anastomoses of the intercostal arteries. Anastomosis is demonstrated, first, by the presence of pulsating arteries on the back in the interscapular area—the posterior scapular, the suprascapular and the subscapular vessels. The excavations of the lower rib margins which are seen in the x-ray film are further proof of the presence of anastomoses of the intercostals.

The cirroid aneurysmal mass in the left rectus muscle marks the anastomosis of the left internal mammary artery with the deep epigastric artery which pours the blood into the arteries of the left leg. The stethographic registration of the thrill also shows the time it requires for the blood to get from the heart to the location of the cirroid aneurysm.

The chest film shows the *great broadening of the transverse diameter of the heart* and the convexity to the right of the aortic shadow. The films from both patients reveal the characteristic contour of the left border of the aorta, with *absence of the aortic knob*. In the oblique film, especially the left oblique, the retro-aortic and retrocardiac spaces are clear areas which normally should be hazy, marking as they normally do the descending arch and upper part of the descending thoracic aorta. In neither patient is there extreme dilatation of the proximal aorta, although the narrowing and kinking in the region of the aortic isthmus can be seen.

PROGNOSIS

A few words should be devoted to the future outlook for these two individuals. They have found encouragement in the case record of Reynaud's patient, a man with coarctation of the aorta who lived to the age of ninety-two, without apparent inconvenience. However, we are well aware that living with such an anomaly is quite hazardous. Termination may be sudden or subacute. Sudden death from intrapericardial or extrapericardial rupture of the aorta may ensue. Dissecting aneurysm for aortic rupture may occur. Cerebral

although the needle moves when the cuff is placed upon the foot, no definite reading can be made.

Stethographic Studies.—An interesting set of stethographic registrations have been made, using rapidly moving electrocardiograms for timing purposes (Fig. 40). Number 1 registers a systolic murmur over the sixth right sternocostal articulation. Number 2, taken at the apex of the heart, reveals presystolic and systolic murmurs with a fainter diastolic murmur. In No. 3, taken at the aortic interspace, the rough aortic systolic murmur with the diastolic murmur is seen. In No. 4, taken over the right carotid in the neck, the long systolic and diastolic murmurs are visualized. The sound bell was placed over the cirroid aneurysm in tracing No. 5 and the late bruit is visible at the time of the T wave in the Lead 2 electrocardiogram. The Lead 2 electrocardiogram was used with all of the stethographic tracings.

Discussion

This patient demonstrates again the fact that the physical examination *alone* supplies sufficient evidence for the diagnosis of coarctation of the aorta. Most of the characteristic features of this anomaly are well illustrated. It is found most often in the male sex, and usually in highly developed individuals of more than average intelligence. The patient usually possesses great energy, ambition and bodily vigor, as evidenced in this instance in which he was found to be working six and often seven days a week.

While the patient's temperature, when taken by mouth, did not show fever, his lower extremities felt cooler than the upper, although no surface temperature readings were made. The *hypertension in the upper extremities* together with *absence of femoral pulsation* and the *inability to obtain blood pressure values in the lower limbs*, is one of the most important features of the anomaly. True it is, that the pressures in the upper limbs indicated aortic regurgitation. However, the absence of pulsation and the absence in the femoral artery of the characteristic vascular features like Duroziez's murmurs and Traube's pistol shot sounds, and toning, indicate that a complicated aortic insufficiency exists. The first personal case described by Dr. Maude Abbott in her "Atlas of Congenital Cardiac Disease," page 20, concerns a case of coarcta-

ischemia. There has been demonstrated an appreciable decrease in renal blood flow even though the glomerular filtration rate is normal. Glomerular efferent arteriolar spasm which is present is *secondary* and compensatory.

TREATMENT

The only treatment indicated is an attempt to prevent the aforementioned modes of termination. Recovery has been described in the subacute bacterial endocarditis which complicates this anomaly.

BIBLIOGRAPHY

1. Stewart, H. J. and Bailey, R. L., Jr.: The Cardiac Output and Other Measurement of the Circulation of the Aorta. *J. Clin. Inv.*, 20: 145 (March) 1941.
2. Friedman, M., Selzer, A. and Rosenblum, H.: The Renal Blood Flow in Coarctation of the Aorta. *J. Clin. Inv.*, 20: 107-111 (March) 1941.
3. Nicolson, G. H. B.: Coarctation of the Aorta in a Child with Arrested Subacute Bacterial Endarteritis and a Calcified Mycotic Aneurysm at the Seat of Stricture. *Am. Heart J.*, 20: 357-365 (Sept.) 1940.
4. Gitlow, S. and Sommer, R. I.: Complete Coarctation of Aorta: Case Report. *Am. Heart J.*, 20: 106-110 (July) 1940.
5. Mendelson, C. I.: Pregnancy and Coarctation. *Am. J. Obst. & Gynec.*, 39: 1014-1021 (June) 1940.
6. Page, I. H.: Effect of Chronic Constriction of Aorta on Arterial Blood Pressure in Dogs; Attempt to Produce Coarctation of the Aorta. *Am. Heart J.*, 19: 218-232 (Feb.) 1940.
7. Baylin, G. J.: Collateral Circulation Following Obstruction of the Abdominal Aorta. *Anat. Rec.*, 75: 405-408 (Nov. 25) 1939.
8. Woodbury, R. A., Murphy, E. E. and Hamilton, W. F.: Blood Pressure in Aortic Coarctation. Study of Pulse Contours Taken by the Direct Method. *Arch. Int. Med.*, 65: 752, 1940.
9. Ingham, D. N.: Coarctation. *New York State J. Med.*, 39: 1865-1870 (Oct.) 1939.
10. Abbott, Maude E.: Atlas of Congenital Heart Disease. *Am. Heart Assoc.*, New York, 1936.
11. Hallack, P. and Hebbel, R.: Coarctation of Aorta, Nonclinical Type; Associated with Congenitally Bicuspid Aortic Valve; Method for Its Recognition, with Report of Case. *Am. Heart J.*, 17: 444-451 (April) 1939.
12. Brothner, R. J.: Etiology of Hypertension Resulting from Coarctation. *Arch. Path.*, 28: 676-696 (Nov.) 1939.
13. Regester, R. P. and Innes, M. B.: Spontaneous Rupture of the Aorta with Hemopericardium Caused by Coarctation. *Am. Heart J.*, 15: 365-69 (March) 1938.
14. Boyd, L. J. and Merblow, S. C.: Coarctation of Aorta; Dissecting Aneurysm and Aneurysmal Dilatation of Left Vertebral Artery. Case. *Arch. Int. Med.*, 11: 845-850 (Nov.) 1937.

hemorrhage due to the hypertension and to the presence of multiple aneurysms of the cerebral vessels is a frequent cause of sudden exitus. Subacute bacterial endocarditis is often encountered, occasionally an acute endocarditis. A few individuals succumb to cardiac failure of the congestive type.

ETIOLOGY

In the introductory paragraph of this clinic we suggested that the various causes of the symptom, hypertension, should be occasionally reviewed. The reference here was to the clinical varieties of hypertension rather than to its causative mechanisms. For example, hypertension may be a symptom secondary to a renal disease like glomerulonephritis. It occurs in various diseases of the endocrine glands, such as tumors of the suprarenals and Cushing's syndrome. Cardiovascular diseases like complete heart block, coarctation of the aorta and aortic regurgitation are accompanied by elevation of blood pressure. A variety of lesions in the intracranial cavity may have the associated symptom of hypertension. Emotional causes induce elevation of pressure.

Today the theory that essential hypertension is the result of a pressor substance liberated by the kidney is more and more widely accepted. In the case of coarctation, the experimental and clinical evidence is interpreted differently by two opposing schools of thought. By one the view is entertained that the hypertension is *mechanical*, the result of obstruction close to the heart. Supporting this is the clinical observation correlated with experimental data that the amount of rise in the blood pressure is roughly proportional to the degree of obstruction of the blood flow. Thus the greater the degree of stenosis, the greater the rise in blood pressure. Vasodilator and vasopressor drugs give equivocal results although the action on the blood vessels of the upper and lower extremities is approximately the same. Experimentally, when aortic obstruction is produced paralleling coarctation, the induction of renal ischemia influences very little the acute hypertension induced by ligation of the aorta.

Another group of investigators believes that the coarctation causes the rise in the blood pressure *by producing renal*

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12. Brochner, R. J.: Etiology of Hypertension Resulting from Coarctation. *Arch. Path.*, 28: 676-696 (Nov.) 1939.
13. Regester, R. P. and Innes, M. B.: Spontaneous Rupture of the Aorta with Hemopericardium Caused by Coarctation. *Am. Heart J.*, 15: 365-69 (March) 1938.
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HODGKIN'S DISEASE; VEGETATIVE AND ULCERATIVE ENDOCARDITIS

Clinical and Pathological Conferences at Cook County Hospital*

WALTER SCHILLER, M.D.†
and
LEROY H. SLOAN, M.D., F.A.C.P.‡

DR. SCHILLER: We are presenting to you this morning a résumé of four patients observed on the Medical Service of the Cook County Hospital and followed through to the post-mortem examination, giving us an opportunity to discuss the clinical and pathological findings.

HODGKIN'S DISEASE

Case I

Our first patient is a forty-year-old white woman who has complained of nervousness and exhaustion for over a year, night sweats for about thirty days, swollen inguinal lymph glands for three weeks, and chills and fever for three days. In the past year the patient has become increasingly nervous and exhausted without presenting sufficient clinical evidence to warrant a diagnosis. During the last four months the tired feeling and exhaustion have become acute. Night sweats have been present virtually every night. A swelling in the right groin has been tender to touch. With the onset of the chills and fever there has developed weakness, aching of the muscles, marked thirst and general apathy. Headaches and dizzy spells have also been present recently. In the past history we find scarlet fever, tonsillitis, pneumonia, measles and mumps. The patient has had two pregnancies, with abortions at two and four months respectively.

* Clinic of Dr. Walter Schiller. Clinical Comment by Dr. LeRoy H. Sloan.

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‡ Professor of Medicine, University of Illinois College of Medicine; Attending Physician, Cook County Hospital.

15. Wechsler, H. F. and Gustadson, E.: Coarctation (Adult Type): Congenital Bicuspid Aortic Valve; Subacute Bacterial Endocarditis. Case. *Am. Heart J.*, 14: 107-112 (July) 1937.
16. Maycock, W. d'A.: Congenital Stenosis of Abdominal Aorta. *Am. Heart J.*, 13: 633-646 (June) 1937.
17. Cookson, H.: Coarctation of Aorta with Toxic Goiter Treated by Complete Thyroidectomy. *Lancet*, 2: 623-625 (Sept. 12) 1936.
18. Graybiel, A., Allen, A. M. and White, P. D.: Histological Study of Arterioles of Muscle and Skin from Arm and Leg in Individuals with Coarctation of Aorta. *J. Clin. Inv.*, 14: 52-56 (Jan.) 1935.
19. Walker, W. G.: Coarctation in Father and Son. *New England J. Med.*, 211: 1192-1195 (Dec. 27) 1934.
20. Lewis, Thomas: Material Relating to Coarctation of the Aorta of the Adult Type. *Heart*, 16: 205-242 (June 14) 1933. Ten plates.

lary line. Multiple adhesions are observed between the gallbladder and the right lobe of the liver. The left *pleural cavity* is completely obliterated by fibrous adhesions. The right pleural cavity has focal fibrous adhesions at the apex. The pericardial sac contains a few cubic centimeters of an amber-colored fluid.

The *heart* weighs 200 gm. The myocardium is extremely soft, and pale purplish red. The left ventricle wall measures 10 mm. and the right 2 mm. The pulmonary artery is 7.4 mm. in circumference. The aorta measures 63 mm. and the intima shows single fatty and hyaline plaques. The endocardium in the supravulvar region is thickened. There is slight thickening of the free edge of the mitral valve. The coronary arteries show a slight thickening of the wall; their lumina are everywhere patent.

The *thyroid gland* weighs 20 gm. It is moderately firm and on section is seen to be light yellowish red and moderately rich in colloid.

The *spleen* weighs 190 gm. Its consistency is diminished and its capsule is thin and smooth. On section it is seen to be light tan-yellow in color, with deep, purple-red acinar centers. There are focal areas of light tan-yellow, firm tissue scattered throughout the liver parenchyma, measuring from 3 mm. up to 30 mm. The liver parenchyma surrounding these areas is bright yellow. There are focal areas which are wedge-shaped and deep purple-red.

The *adrenals* weigh 24 gm. They are soft. The cortex is bright yellow and measures 1 mm. The medulla is liquefied.

The perigastric and the peripancreatic *lymph nodes* are enlarged up to 15 mm. in diameter, stony hard and on section are light tan with many hemorrhages present.

The hilar lymph nodes of the liver and at the junction of the cystic and hepatic ducts are similar.

The *pancreas* weighs 100 gm. It is soft and on section is light yellowish tan and uniformly lobulated.

The pleural surface of the *left lung* is thickened throughout and all lobes are crepitant. On section both lobes are light purple-red and slightly moist with a frothy fluid. The mucosa of the bronchi is light reddish tan with a thin mucoid material covering the tissue. The peribronchial lymph nodes of the hilum, up to 12 mm., are moderately firm and anthracotic. The *right lung* shows a smooth and glistening pleural surface. All the lobes are crepitant and on section they are light reddish gray and slightly moist. The mucosa of the bronchi and the hilar lymph nodes are similar to the left lung.

Physical Examination

On admission to the hospital general examination revealed a patient who was seriously ill. The temperature, however, was only 98.6° F. at the time of the actual examination. There were many discrete, somewhat tender, small cervical lymph glands. The axillary and supraclavicular glands were enlarged, discrete and tender. Examination of the heart disclosed no abnormalities, and the lungs were also normal. The liver was enlarged one fingerbreadth below the costal margin. No palpable masses were found in the abdomen, and there was no tenderness. The spleen was not palpable. The inguinal glands were enlarged, more on the right side than on the left, and were, in general, discrete and freely movable though occasionally a matting together had occurred. Seven days after admission the patient developed petechial hemorrhages in the gums, tenderness over the liver, distention of the abdomen, elevation of temperature; she became progressively stuporous and died.

Laboratory Studies

Hematologic examination revealed 69 per cent hemoglobin, 3,730,000 red cells, 2100 white cells, with a differential count of 95 per cent polymorphonuclear leukocytes, 4 per cent lymphocytes and 1 per cent myelocytes. The Wassermann blood test was negative. Urinalysis was essentially negative. The nonprotein nitrogen of the blood was moderately elevated as was also the uric acid. The last hematologic examination was reported as showing a moderate hyperplasia of the bone marrow and developmental arrest of the granulocytes at the myelocyte stage, with a marked displacement of the erythroid series.

Postmortem Examination

The body is that of a slenderly built, white female. The skin over the entire body is slightly icteric. The conjunctiva is yellow-tan and slightly edematous. The mucosa of the lips and mouth is purplish tan. The fingernails are cyanotic. The lymph glands of the neck are slightly enlarged. There are multiple subcutaneous petechiae especially in the upper and lower extremities and on the neck and the chest. There is a slight pitting edema of both lower extremities.

The *liver* extends 8 cm. below the right costal margin. There is 1000 cc. of a clear amber-colored fluid in the peritoneal cavity. The lower pole of the *spleen* is at the eleventh rib, posterior axil-

lary line. Multiple adhesions are observed between the gallbladder and the right lobe of the liver. The left *pleural cavity* is completely obliterated by fibrous adhesions. The right pleural cavity has focal fibrous adhesions at the apex. The pericardial sac contains a few cubic centimeters of an amber-colored fluid.

The *heart* weighs 200 gm. The myocardium is extremely soft, and pale purplish red. The left ventricle wall measures 10 mm. and the right 2 mm. The pulmonary artery is 74 mm. in circumference. The aorta measures 63 mm. and the intima shows single fatty and hyaline plaques. The endocardium in the supraventricular region is thickened. There is slight thickening of the free edge of the mitral valve. The coronary arteries show a slight thickening of the wall; their lumina are everywhere patent.

The *thyroid gland* weighs 20 gm. It is moderately firm and on section is seen to be light yellowish red and moderately rich in colloid.

The *spleen* weighs 190 gm. Its consistency is diminished and its capsule is thin and smooth. On section it is seen to be light tan-yellow in color, with deep, purple-red acinar centers. There are focal areas of light tan-yellow, firm tissue scattered throughout the liver parenchyma, measuring from 3 mm. up to 30 mm. The liver parenchyma surrounding these areas is bright yellow. There are focal areas which are wedge-shaped and deep purple-red.

The *adrenals* weigh 24 gm. They are soft. The cortex is bright yellow and measures 1 mm. The medulla is liquefied.

The perigastric and the peripancreatic *lymph nodes* are enlarged up to 15 mm. in diameter, stony hard and on section are light tan with many hemorrhages present.

The hilar lymph nodes of the liver and at the junction of the cystic and hepatic ducts are similar.

The *pancreas* weighs 100 gm. It is soft and on section is light yellowish tan and uniformly lobulated.

The pleural surface of the *left lung* is thickened throughout and all lobes are crepitant. On section both lobes are light purple-red and slightly moist with a frothy fluid. The mucosa of the bronchi is light reddish tan with a thin mucoid material covering the tissue. The peribronchial lymph nodes of the hilum, up to 12 mm., are moderately firm and anthracotic. The *right lung* shows a smooth and glistening pleural surface. All the lobes are crepitant and on section they are light reddish gray and slightly moist. The mucosa of the bronchi and the hilar lymph nodes are similar to the left lung.

The *kidneys* together weigh 300 gm. Their consistency is increased. The capsule strips with ease leaving a smooth brown-tan surface. On section the cortex measures 8 mm. and the markings are distinct.

The *urinary bladder* presents a light yellow-tan, moderately trabeculated mucosa.

The *cervix* is light tan; a dark, purple-red, blood-tinged, muroid material can be expressed. The cervical canal is filled with blood-tinged mucinous material. In the fundus of the uterus is a dark purple-red submucous fibroid measuring $2\frac{1}{2}$ by 1 by 2 cm. There are several intramural fibroids up to 5 mm. in diameter. The fimbriated ends of both fallopian tubes are occluded and filled with a clear serous fluid.

The *leptomeninges* over the frontal and the parietal lobes show a mild diminution in transparency in the form of very fine whitish streaks. The vessels at the base do not appear significantly atherosclerotic. Serial slides through the *brain* stem and cerebellum reveal no significant abnormalities, except for a small multilocular cyst formation in the choroid plexus at the beginning of the posterior horn of the right lateral ventricle.

Anatomical Diagnosis

1. Hodgkin's lymphogranulomatosis involving the perigastric, peripancreatic, porto-biliary and iliac lymph nodes.
2. Hodgkin's infiltration of the liver.
3. Brown atrophy of the myocardium with marked dilatation of the cardiac chambers.
4. Marked cloudy swelling and passive congestion of the liver and the kidneys.
5. Slight passive congestion of the lungs.
6. Primary tuberculous complex of the left upper pulmonary lobe.
7. Bilateral hydrosalpinx.
8. Infarcted pedunculated polyp of the fundus of the uterus.
9. Icterus.
10. Icteric nephrosis.

Microscopic Pathology

The *brain* presents a mild degree of fibrous tissue hyperplasia. The ganglion cells in some places show degenerative changes, some of them corresponding to the picture of a chronic ganglion disease, and others to that of simple ganglion cell disease. These

changes are associated with slight glial proliferation affecting chiefly oligodendroglia.

The *kidney* presents congestion of glomerular tufts with granular degeneration of tubular epithelium.

The *myocardium* shows a moderately distinct striation of cells and brown pigment at both poles of the nuclei. There is a slight fatty infiltration in the muscle cells.

The *spleen* shows large, distinct and sharply demarcated lymph follicles consisting of large lymphocytes without germinal centers. The sinusoids are stuffed with blood and the pulp is similarly congested with red blood cells. The lymph nodes present numerous eosinophilic leukocytes, and red-staining necrotic material with pyknotic nuclei. There are numerous large oval cells, the protoplasm of which consists of deep, red-staining, granular masses. There are a few Dorothy Reed giant cells. The infiltration of the lymph nodes extends to the adjacent fat tissue.

The *liver* presents in the central parts of the acini a hemorrhagic necrosis with moderate passive congestion. The necrotic liver cells contain a few brown bile pigment granules and still more of these granules can be seen in the Kupfer cells which present a pyknotic nucleus. The periportal fields are small and surrounded by dense infiltration of large numerous monocytes and some leukocytes. This infiltration extends into the stroma of the periportal fields. Where the liver cell trabeculae are preserved the sinusoids contain, with the normal red blood corpuscles, large monocytes similar to the infiltrating cells described above.

Case II

Our second patient is a *white man, twenty years of age*, who came into the hospital complaining of shortness of breath and loss of 50 pounds in weight within the last eleven months. He was quite well until about eleven months ago when he became dyspneic on slight exertion, and shortly thereafter even when at rest. He was in the hospital seven months, during which time the dyspnea and orthopnea became so marked that it was necessary to aspirate the chest on three different occasions. A yellowish watery fluid with a low specific gravity was removed. X-ray treatments were given. There was no history of rheumatic fever. The patient complained of marked sweating but there was no cough or edema of the feet or ankles.

Examination and Hospital Course

On admission, examination showed a man of fair general nutrition, very white and pale. The fingernails and toenails were cyanotic. The chest was emphysematous and of the conformation known as "pigeon breast." In the supraclavicular fossa on both sides was an almond-sized gland; smaller discrete, walnut-sized glands were easily palpable and freely movable in both axillary areas. The epitrochlear, cervical and inguinal glands were not enlarged above the normal. The heart borders were easily made out, but the cardiac dullness was increased both to right and left. The tones were muffled and distant, the rhythm regular, and no murmurs were heard.

The temperature on admission was 100.2° F., pulse rate 120, and respiratory rate 26, but during the patient's sojourn in the hospital his temperature curve oscillated between 98° and 103° F. The blood pressure was 110 mm. of mercury systolic and 50 diastolic.

A pericardial tap was attempted lateral to the apex but no fluid was obtained. An axillary lymph node was removed for *biopsy*. The Mantoux test was entirely negative. Paracentesis of the left chest returned 60 cc. of straw-colored fluid.

The patient failed rapidly, complained of much precordial pain, dyspnea and weakness and expired suddenly.

Laboratory Studies

The laboratory findings showed nothing significant in the urine except a few white blood cells. The hemoglobin was 60 per cent, red blood cells 3,920,000, and white blood cells 12,000 to 16,000. The differential count showed 81 per cent polymorphonuclear leukocytes, 15 per cent lymphocytes and 4 per cent monocytes. X-ray of the chest was reported as showing a pericardial effusion with marked passive congestion. Sputum tests revealed no tubercle bacilli. Wassermann and Kahn reactions were both negative. The electrocardiogram was reported as showing myocardial damage, slight right axis deviation, and sinus tachycardia. Nonprotein nitrogen of the blood was 33 mg. and creatinine 1.1 mg. per 100 cc.

Postmortem Examination

The body is that of a well developed, well nourished, white male. The skin is white and pale. Conjunctivae are pale, but the fingernails and toenails are cyanotic. There is no pitting edema.

In both axillary regions are firm, easily palpable lymph nodes the size of a chestnut on the right, of a cherry on the left. There is a slight bulging of the intercostal spaces especially of the lower thorax.

The *peritoneal cavity* is free. The peritoneal serosa is smooth and shiny, and the liver and spleen are unchanged. Upon remov-



Fig. 41 (Case II).—The small drop heart is encased by a thick, circular, white, resistant mass of the firm granulation tissue which extends between the pericardium and the mediastinal pleura. It includes several lymph nodes which are infiltrated by the same specific granulation tissue, but still well demarcated from the mass. On both sides at the top the darker staining, compressed upper lobes of the lungs can be seen.

ing the sternum a *thick, solid, white, fibrous mass* appears which extends around the pericardial sac and is attached in the front to the sternum and on both sides to the mediastinal pleura. This white firm mass is 8 to 12 cm. thick, and completely encapsulates the pericardial sac (Fig. 41). The *heart* lies in the center of this mass, like the stone in a cherry. In the left part of this mass are

several, large, smooth-walled cavities within the tumor mass which contain a slightly turbid, brown, serous fluid. In the inferior and posterior parts the mass is stony hard and can be separated only with difficulty from the diaphragms, the vertebral column, and from the articulating parts of the ribs.

Both *pleural cavities* are completely obliterated, and the *lungs* are compressed by the mediastinal mass. In the left upper pleural cavity is an encapsulated pleural effusion of a light yellow, turbid fluid amounting to 400 cc. The *bronchial* and *peritracheal lymph nodes* are markedly enlarged up to 3 cm. in diameter, and on section are white, homogeneous and fibrotic. The *myocardium* is flabby, contracted and pale purplish red. Both *lungs* are compressed and on section pinkish gray in color, moist, and free from foreign tissue.

The *liver* weighs 1500 gm., its capsule is thin, consistency soft, and color dark brown with moderately distinct markings of passive congestion. The *spleen* weighs 180 gm., its capsule is smooth, gray and the consistency soft; on section it is dark purplish brown and the lymphoid follicles are small and distinct. The *pancreas* weighs 90 gm. It is soft and on section is purplish gray with a few pinhead-sized areas of fat necrosis. The other abdominal organs, the ductless glands and the brain show no pathologic conditions with the exception of the periaortic lymph nodes which are enlarged to a diameter of 3 cm. and on section are grayish white and firm.

Microscopic Examination

The enlarged *lymph nodes* present a marked increase in the reticulo-endothelial cells. The main part of the parenchyma consists of a fibrous granulation tissue which in many parts shows a diminished number of nuclei and progressive fibrosis (Fig. 42). There are focal accumulations of lymphocytes and leukocytes, and a great number of Dorothy Reed giant cells. No eosinophil leukocytes are present. This characteristic *Hodgkin's granulation tissue* extends beyond the capsule in several of the lymph nodes (Fig. 43). The matted lymph nodes are embedded in a mass of granulation tissue, yet are sharply demarcated within the mass. The tissue surrounding the pericardial sac is of a similar nature and here, too, in the interior part several lymph nodes can be seen which are embedded in the granulation tissue but are still sharply demarcated. The fibrous tissue component of the mediastinal and pericardial mass is much more prominent than in any



Fig. 42 (Case II).—The granulation tissue of the pleuropericardial space is concentrically arranged in the center around a small arteriole; it consists of fibroblasts, lymphocytes, monocytes and a few leukocytes. Beginning hyalinization is seen on the right.

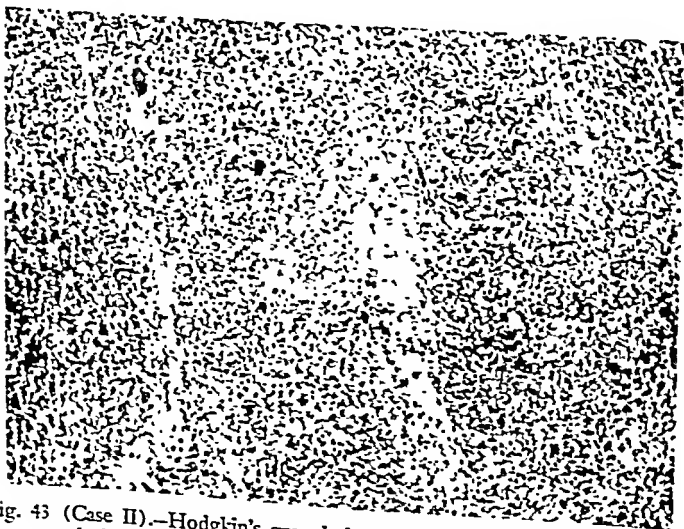


Fig. 43 (Case II).—Hodgkin's granulation tissue from a mediastinal lymph node is composed of the same elements and a few giant cells.

other areas, but is less cellular and more compact. There are accumulations of lymphocytes, large monocytic elements and scattered leukocytes.

The *liver* presents moderate passive congestion by diffuse dilatation of the sinusoids around the central veins, with compression of the innermost part of the liver cell trabeculae. The stain for fat reveals that the Kupfer cells are stuffed with sudanophilic droplets. The *spleen* presents small, distinct lymph follicles, the trabeculae are thin, and the sinusoids are stuffed with red blood cells. The pulp is slightly fibrotic. The remaining tissues show no pathologic changes.

Anatomical Diagnosis

1. Hodgkin's disease involving the mediastinum, the space between the pleura and pericardium, both pleural cavities, and the superior aspect of the diaphragm.
2. Exudate in the left pleural cavity with compression atelectasis of the left lung.
3. Hodgkin's disease of the axillary lymph nodes on both sides, and of the periaortic, the abdominal, the bronchial, the tracheal and the pulmonary hilar lymph nodes.
4. Involution of the heart.
5. Passive congestion and parenchymatous degeneration of the liver.

Pathological Discussion

The diagnosis in these cases was confirmed by the only reliable method known, namely histologic examination of excised tissue. The classical picture of Hodgkin's disease is unmistakable, but the early picture may be so lacking in specific, confirmatory evidence as to make possible only a tentative diagnosis.

In our second patient a specific tissue bearing the characteristics of granulation tissue spread in a preformed space between the pericardium and the mediastinal pleura without invasion of the walls. The process involved the lymph nodes which are connected to the primary focus by lymph vessels. This method of propagation is found in many inflammatory infections as well as in carcinomatous and other neoplastic deposits. On the other hand, there is no other process which

produces such extensive masses of granulation tissue between neighboring serous membranes as the specific lymphogranulomatous lesion of Hodgkin's disease.

While the pathological picture at times gives one the impression of a neoplastic tumor, most pathologists agree that, taking into consideration the larger histologic and clinical characteristics, this disease is an inflammatory one in which the whole reticulo-endothelial system is involved.

Clinical Discussion

DR. LEROY H. SLOAN: Hodgkin's disease is a fairly common condition here at the County Hospital. At times the diagnosis can be well established on the history alone, while occasionally it is entirely impossible except at autopsy and after very careful microscopic examination of many sections of tissue. There has long been disagreement as to whether Hodgkin's disease is a *tumor* or is due to acute and chronic *inflammatory reactions* of the reticulo-endothelial tissue. Apparently the pathologists are well agreed that Hodgkin's disease is an inflammatory reaction of such tissue to a toxic process and is not a true neoplasm, but as clinicians we are all struck with the great similarity of the disease to malignant tumor growth. However, when one sees the very toxic reaction of a patient to generalized Hodgkin's disease, and when he notes the characteristic Pel-Ebstein fever, he is impressed with the probable inflammatory character of the lesion.

We should dismiss the idea that Hodgkin's disease is a disease purely of a set of lymph glands of a particular portion of the body, although the average patient will come in complaining of the enlargement of a gland either of the neck, the supraclavicular area, the axilla, the inguinal area or perhaps of enlargement of the spleen. We do see instances occasionally in which the process seems to be limited strictly to the internal glands and organs, but ordinarily it is likely that cervical and axillary glands are but the signal of mediastinal involvement and inguinal glands but the external evidence of abdominal involvement.

Clinical Features of Hodgkin's Disease

Our patients generally are relatively young, between the ages of twenty and forty, with perhaps the majority between twenty and thirty years of age. Males predominate. The most frequent complaint is of *enlargement of a gland* commonly in the neck, the supraclavicular area, the axillary area or the inguinal area. The enlarged glands are discrete, and freely movable, are not matted together until very late, and are generally the size of a pea or walnut, although they may reach huge proportions. They are usually bilateral.

The *spleen* is enlarged in at least 60 per cent of the patients and the *liver* in from 40 to 50 per cent. Early the condition is *glandular*, that is, its principal features are enlargement of glands and compression of organs. Later the picture may become that of a blood dyscrasia, of a septic undisclosed fever, of a paraplegia, of compression of cerebral structures, of blockade of the outlet of the stomach, of a nephrosis-like syndrome with amyloidosis, edema, anasarca, pleural effusion, pericardial effusion and ascites.

Other complaints of the patient with Hodgkin's disease are progressive *weakness*, *exhaustion*, recurrent bouts of *fever*, loss of weight, *dyspnea*, orthopnea, *profuse sweating*, *pruritus*, cough, and pain due to compression of nerves and blood vessels, enlargement of the abdomen, chills and edema of the feet, ankles and later of other structures.

On *physical examination* the patient may appear to be entirely normal except for the glandular increase, or he may present a most miserable picture of toxic exhaustion with pallor, edema, petechial hemorrhages, cyanosis, orthopnea and so on. The *blood picture* unfortunately is not characteristic. We all look for the early eosinophilia but too often find it absent.

Diagnostic Criteria

The only reliable method of absolute diagnosis is *biopsy*, that is, the removal of a characteristically typical gland (one which is sufficiently enlarged and discrete and known to have recently enlarged) and microscopic examination of such a gland by a competent pathologist. As in all other procedures,

experience in examining such glands is very necessary, but even in the most expert hands the tissue taken in early Hodgkin's disease may appear to be of a nonspecific type. In this hospital we have learned to be biopsy conscious as a result of Dr. Jaffe's constant stimulation. Perhaps we get a bit too enthusiastic at times but the principle of "better a look than a guess" is incontrovertible.

The *Gordon test* is occasionally helpful in the diagnosis. This is carried out by emulsifying the removed gland in sterile saline and injecting the material into the brain of a rabbit. A positive test is evidenced by encephalitis and ataxia. However, this test is not specific but is a response to the eosinophilic cells and perhaps we shall have to discard it.

A neglected test which is easily available is of the *basal metabolism*, which is increased sufficiently often to be of real service, particularly in suspected abdominal Hodgkin's disease. In fact, given a fairly normal blood count, the aforementioned symptoms, persistent fever and nothing pathognomonic, Hodgkin's disease is well worth careful consideration.

One of the most interesting associations in Hodgkin's disease is the *Pel-Ebstein fever*. This fever is cyclic and recurrent; it reaches a maximum in about three days, hangs at a high peak for about three days, then returns in about three days to a normal, the cycle thus occupying roughly ten days (at times fourteen days). For about the same number of days there is little or no fever, then the cycle begins again. This fever cycle seems to have no good reason for beginning or for ending, but it does impress the clinician with the general inflammatory nature of what he has perhaps been considering a localized glandular process. It suggests that there is taking place a reaction of the reticulo-endothelial structures to a toxin or a foreign protein, and helps to emphasize the lymphogranulomatous and reticulo-endotheliosis-like nature of the underlying process.

How long does the pathologic process of Hodgkin's disease go on? Experience in this vicinity would make the period from six to twenty-four months, but in the literature the process has been as acute as one month, and in private practice as long-continued as several years. The pruritus,

the sweating, the elevation of the basal metabolism, the involvement of the skin with urticaria, with pigmentation, and with secondary results of pruritus all show how closely the process may be linked with the leukemias—to say nothing of the actual appearance and feel of the glands themselves. The neurologist sees Hodgkin's disease as an infiltrating process or compression syndrome which may produce a paraplegia, or isolated cranial nerve palsy, or symptoms thought characteristic of localized brain tumor. The orthopedist may see the condition as a sclerosing osteitis of the spinal vertebrae or an osteoclastic process. The dermatologist may see a picture of urticaria, pruritus and other features which appear to be quite limited to the skin.

Treatment of Hodgkin's Disease

Opinion is divided on the real benefits of x-ray and radium therapy, but I am sure that all of us would prefer that careful and skillful therapy be given rather than that we depend upon the do-nothing policy advocated at one time or another. I am sure that many of the distressing symptoms of this disease can be promptly relieved by x-ray or radium therapy, and that patients can be made much more comfortable for considerable periods.

Perhaps the newest attack by irradiated phosphorus may be of real value in Hodgkin's disease and its closely allied condition, leukemia. Time will tell. For combating the anemia, the sweating, the exhaustion and the pruritus one may employ symptomatic treatment, but most of these symptoms will disappear as the generalized granulomatous endotheliosis disappears following x-ray therapy. Transfusions, nutritious diet and iron, liver, vitamin, arsenic and ultra-violet therapy, all have a place in the management of these patients.

VEGETATIVE AND ULCERATIVE ENDOCARDITIS

Case III

The patient, a fifteen-year-old Negro girl, entered the Cook County Hospital complaining of severe headache, which had been present for three days. On the third day this headache

became so severe that she was forced to remain in bed. On attempting to rise from bed her limbs would become numb and limp. She had a mild convulsive seizure and collapsed, but was not unconscious at any time. On one occasion she attempted to rise and walk, but was unable to do so, and had to be carried back to bed. She began to vomit all food and liquid intake. On the morning of admission she had several chills associated with epistaxis. The headache did not respond at any time to ordinary medication. She was a known cardiac patient and had been attending a special school for cardiac patients. About a year ago she had a similar but less severe attack. The onset of the rheumatic fever was at six years.

Examination and Hospital Course

On admission to the hospital the patient's temperature was 99.2° F., pulse 80, respiratory rate 24, blood pressure 150 mm. of mercury systolic and 40 diastolic. The principal observations were stiffness of the neck, postoccipital tenderness, enlargement of the heart to the left, a rough systolic murmur heard over the entire cardiac area and an irregular heart rate.

Twelve hours after admission the patient became comatose, frothy fluid issued from the nose and mouth, and there were slight tonic convulsive seizures. The apical rate thirty minutes later was 188; she became markedly cyanotic with shallow respirations, and expired.

The laboratory findings were without significance, except for the presence of hypochromasia with anisocytosis. The Wassermann test was negative.

Postmortem Examination

The body is that of a well-nourished, Negro female. There is no pitting edema. The mucosa of the conjunctiva, lips and mouth is pale.

There has been a postmortem digestion of the fundus of the stomach and gastric contents are in the left upper quadrant. The capsule of the spleen is covered by this dirty brown material. The intestinal loops are slightly distended with gas. The midline fat is 17 mm. The liver extends 55 mm. below the xiphoid process and is at the right costal margin. The right diaphragm is at the fourth intercostal space. The right pleural cavity is free and the left pleural cavity contains 400 cc. of a turbid brown, serous

fluid. The pericardial sac contains 40 cc. of a similar dark, purple brown fluid. The mucosa of the esophagus is thickened and white. The submucosal veins are moderately dilated. The thymus weighs 31 gm. and is pale, grayish tan and lobulated.

The *heart* weighs 410 gm. The ventricles are markedly dilated and hypertrophied. The right ventricle is well contracted and its myocardium is firm and pale pink. The left ventricle measures 17 mm. and the right ventricle 2 mm. thick. The pulmonary artery measures 80 mm. and the aorta 62 mm. in circumference. The free margin of the mitral valve is covered with firm, pinkish gray, verrucous precipitations. There are also similar vegetations on the endocardium of the left auricle. The greatest portion of the middle leaflet is ulcerated and there is present a perforation measuring 28 by 9 mm. The chordae tendineae are of normal length and slightly thickened. The aortic leaflets are slightly thickened at the free margins, but otherwise unchanged. The remaining valves are free. The coronary arteries are thin-walled and smooth and their lumina are patent.

The left *lung* shows a few adhesions between the two lobes and the apex is free. On section it is dark, purple-gray and slightly moist, with a few subpleural pinhead-size petechiae. The mucosa of the bronchi is light tan and is covered by a blood-tinged mucoid material. The lymph nodes of the hilus are anthracotic and soft. The right pleural cavity is free. All the lobes are feathery and crepitant. On section it is light pinkish gray and slightly moist with a frothy, blood-tinged fluid.

The *thyroid* weighs 320 gm. and is moderately firm. On section it is grayish tan and homogeneous.

The *spleen* weighs 320 gm. Its capsule is gray, slightly thickened and of soft consistency. On section it is purple-brown with numerous distinct lymphoid follicles.

The *stomach* is moderately contracted. The mucous membrane is pale gray. The folds and rugae are moderately prominent. The fundus is absent as a result of postmortem digestion.

The *pancreas* weighs 60 gm. It is soft and lobulated and upon section is a grayish tan in color.

The *kidneys* weigh 320 gm. The left kidney is firm and the capsule strips with ease leaving a grayish tan, smooth surface. On section the cortex measures 10 mm. and the markings are distinct. The pyramids are dark and purple-red, and the pelvis is grayish white and smooth. The right kidney is similar to the left. The *urinary bladder* contains a few cubic centimeters of a slightly

turbid, yellow urine. The mucous membrane is pale, gray-pink and smooth. The *vagina* is smooth and gray-tan. The *cervix* is smooth and white, with a circular fold at the anterior lip. The *uterus* measures 80 by 50 by 30 mm.; the endometrium is thin, pale purplish gray and smooth. The *fallopian tubes* are slightly elongated (12 cm.), thin-walled and convoluted. The right *ovary* measures 35 by 21 by 16 mm. and on section is seen to contain a few small follicles. The left ovary is similar. The rectum is moderately dilated and the mucosa is pale yellowish gray and thin.

The *liver* weighs 1380 gm. The capsule is thin and on section markings are of a distinct pale and purple-gray.

The *gallbladder* contains 20 cc. of a thin, greenish-black bile. The mucous membrane is dark green and thin. The *adrenals* weigh 9 gm. and are soft. The cortex measures less than 1 mm. The medulla is light gray and soft. The mucosa of the *small intestine* is grayish green. The folds are high and lymphoid follicles in the lower ileum are large and distinct. The Peyer's patches are elevated and distinct. The *large intestines* are dilated, the mucous membrane is light gray and the lymphoid follicles are hypertrophied.

The *brain* of the left hemisphere contains varying amounts of blood in the subarachnoid space. There is a hemorrhagic exudate, 1 mm. in thickness, over the base of the brain covering the pons and continuing into the mesencephalo-cerebral angle. The center of the left cerebral hemisphere shows a large softened area 4 cm. in diameter, which contains clotted blood. The softening in the left hemisphere has completely destroyed the basal ganglia and most of the central white matter. The brain stem and cerebellum proper show no gross abnormalities. There is a vein in the superior frontal sulcus which is large and distended with a thrombus.

Microscopic Pathology

The *heart* muscle fibers present a variety of pale, swollen, and dark shrunken nuclei. The interstitial septa are edematous and many of them contain typical Aschoff nodes, large cells with basophilic protoplasm and some giant cells. The Sudan III stain reveals no fat deposits. The mitral valve is markedly thickened as a result of proliferation of fibrous tissues and also an increased vascularity. The surface of the valve shows a marked necrosis and is infiltrated by polymorphonuclear and round cells immediately beneath the necrotic area. There is a marked prolifer-

ation of young fibroblasts beneath the necrotic and inflammatory area.

The *kidneys* present many enlarged glomeruli which exhibit a marked increased cellularity. Some show hyalinization, some proliferation of Bowman's epithelium. There is a moderate round cell infiltration around a number of the glomeruli. Some of these tubuli adjacent to the glomeruli are filled with red blood cells and in general the tubular epithelium is swollen and slightly granular. The small arterioles show a thickening of the intima and media, mostly by edema.

The *lung* shows some alveoli filled with red blood cells and fibrin. The interstitial capillaries are dilated and stuffed with red blood cells.

The *thymus* reveals a diffuse distribution of the lymphoid cells and numerous Hassal's corpuscles. The *liver* cells are swollen. The sinusoids are dilated and congested with red blood cells. The Disse spaces are markedly enlarged and filled with pale-staining protein material, and the Sudan III stain reveals no fat deposit.

The *spleen* presents numerous large lymphoid follicles which consist almost entirely of germinal centers. The sinusoids are dilated and filled with red blood cells.

The *brain* reveals a dense infiltration of the subarachnoid space, especially within the depths of the sulci, with erythrocytes. In one of these sulci the wall of a thin leptomeningeal vein is densely infiltrated with lymphocytes and numerous polymorphonuclear leukocytes. The adjacent cortex contains scattered fresh petechial hemorrhages. The wall of the vein is disintegrated. In this area the white matter has a spongy, seminecrotic appearance.

Anatomical Diagnosis

1. Acute rheumatic pancarditis.
2. Acute ulcerative and vegetative endocarditis of the mitral valve.
3. Acute hemorrhagic softening and subarachnoid hemorrhages in the left cerebral hemisphere resulting from multiple septic emboli.
4. Hypertrophy and dilatation of the cardiac chambers, especially the left.
5. Beginning hemorrhagic bronchopneumonia in the right lower pulmonary lobe.
6. Hemorrhagic pleural effusion in the left pleural cavity,

with moderate compression atelectasis of the left lower pulmonary lobe.

7. Petechial hemorrhages of the pleura of both lower lobes.
8. Passive congestion of the spleen, liver and kidneys.
9. Infectious hyperplasia of the spleen.
10. Status thymicolymphaticus with persistent thymus, narrowed aorta, and hyperplastic lymphatics of the spleen and intestines.
11. Infantilism of the fallopian tubes.
12. Postmortem digestion of the fundus of the stomach.

Pathological Discussion

This patient presents many of the features of a typical rheumatic infection followed by a terminal endocarditis of infectious type. The onset of her difficulties was at six years of age, and thereafter for nine years, until her death, she was under special cardiac management and protected by special arrangement as to schooling. Her exitus is a result of rheumatic and ulcerative endocarditis, emboli, cerebral softening associated with such emboli, subarachnoid hemorrhage and a general infection.

In children the interval between the onset of rheumatic endocarditis and vegetative ulcerative endocarditis is shorter than in adults. After rheumatic endocarditis one is dealing with a period of more or less compensated heart failure, with fibroplastic deformity of the mitral valve, which usually results in the well known mitral insufficiency or stenosis or both. From such valves or from the endocardium benign emboli commonly arise, and mural thrombi form as a result of the deformity of the valve and are thrown out into the general circulation. The rheumatic endocarditis was still in full activity in our patient. Aschoff nodes were present in the myocardium. Vegetative endocarditis with such a high degree of ulceration shows such activity.

There are three types of fatal outcome in rheumatic infections: (1) during the acute phase of rheumatic pancarditis and its associated joint changes; (2) by decompensation during the phase of chronic fibroblastic deformity of the valve; and (3) by superimposed acute vegetative endocar-

ditis which usually occurs during this phase of fibroblastic deformity. A large number of patients reach compensation but contract a secondary *Streptococcus viridans* infection by way of the tonsils and nasopharyngeal lymphatic tissues. Streptococci in the blood stream attack the already weakened endocardium of the mitral valve, causing an acute vegetative endocarditis. Rheumatic infection involves primarily the myocardial septa and the endothelial cells of the endocardium, the endothelial lining of the joint articulations and eventually of the blood capillaries. A culture of the spleen of our patient showed *Streptococcus viridans*.

Case IV

Our last patient this morning is a white male aged *seventy-seven years* who on admission gave a history of a chill two weeks previously lasting for a half day and followed by fever, cough, substernal pain and dyspnea. He expectorated a brownish material. He complained of no particular pleural pain and had been quite well up to the onset of his present complaint.

Examination and Hospital Course

On examination his temperature was 103° F., respirations 30, pulse rate 120, blood pressure normal. Examination of the lungs disclosed only those minimal findings which might be associated with a scattered bronchitis. The heart was of normal size, with normal rhythm and pulse. No murmurs were heard. The liver was one fingerbreadth below the level of the xiphoid process. X-rays of the lungs showed no consolidation. A diagnosis of acute bronchial pneumonia in an elderly patient was made and he was given sulfathiazole. There was no response. He became very toxic and comatose, with a temperature of 105° F. There was some question as to the presence of petechial hemorrhages in the conjunctiva. Three days after admission the patient succumbed.

Laboratory Studies

Examination of the urine, blood, nonprotein nitrogen and creatinine was of no significance. The blood uric acid was 5 mg. per 100 cc. Hemoglobin was 62 per cent, red cells 3,770,000, white cells 13,300. Differential blood count showed 89 per cent

polymorphonuclears, 6 per cent lymphocytes, 4 per cent monocytes, and 1 per cent undifferentiated cells.

Postmortem Examination

The principal findings are in the *heart* (Fig. 44). The pericardial sac contains a few cubic centimeters of turbid, serous fluid. The right pleural cavity is obliterated by fibrous adhesions. The heart, which weighs 460 gm., is slightly enlarged and the



Fig. 44 (Case IV).—Because of the short duration of this acute endocarditis the ventricles are not thickened. Of the three aortic leaflets the left which is split shows only moderate sclerotic thickening of the intima. The right and the posterior leaflets along the free margin and the adjacent internal parts are covered by finely, adherent, moderately soft, gray, fibrinous, and red hemorrhagic vegetations. The lateral margins of the posterior leaflet are free.

myocardium is pale pinkish brown, soft and flabby. The left ventricle measures 15 mm., the right 2 mm. Numerous petechiae are found in the epicardium of the left ventricle. The free margins of the mitral valve show atherosclerosis. The circumference of

the aortic valve is 70 mm., and the free margins, particularly the posterior and the left, have been destroyed by extensive ulcerations containing heaped-up, irregular, soft masses of mushy, deep purple-red vegetations. The aortic arch shows focal atherosclerotic thickening of the intima. The pulmonary and tricuspid valves are normal.

Numerous pinpoint to pinhead sized, light purple-red submucous petechiae are found in the *stomach*, mostly in the fundus. Numerous petechiae are found in the mucosa of the *gallbladder*. The *kidney* exhibits numerous sharply demarcated, subcapsular cortical infarcts. The mucosa of the *pelvis* reveals a few small petechiae. Numerous petechiae are found in the fundus of the *bladder*.

Microscopic Pathology

The myocardial muscle fibers present slightly indistinct cross striations and a large amount of brown pigment granules at the poles of the nuclei. The interstitial septae are broad and slightly edematous and contain here and there a single leukocyte or lymphocyte. The vegetations of the aortic leaflets consist of a dense network of fibrin with red blood corpuscles and leukocytes in the meshes. There has been an early organization of the vegetations to the stroma of the leaflets by a down-growth of fibroblasts and capillaries. The kidneys present triangular infarcts of subacute necrosis with poorly stained nuclei. The cellular elements of the tubulae and glomeruli are still distinct. The borderline zone of the infarct exhibits a dense infiltration of leukocytes with pyknotic nuclei. In the center of the infarct are focal areas of leukocytes with pyknotic nuclei arranged around necrotic glomeruli, which present one or two capillary tufts filled with deep violet-staining, finely granular masses of cocci. In the cortex outside the infarcted areas are many completely hyalinized glomeruli with increased interstitial fibrous tissue and atrophic tubules around them corresponding to a mild nephrosclerosis. The interstitial blood vessels are dilated, and filled with red blood cells.

Pathological Discussion

This patient presents a somewhat atypical valvular endocarditis representing both vegetative and ulcerative changes. *The importance of this autopsy is to point out that while we assume that young adults may have vegetative and ulcerative and subacute endocarditis we do not commonly regard*

with more than slight suspicion the possibility of such a diagnosis in a patient of seventy-seven years who has had very few if any symptoms until the onset of this terminal episode. I believe that in this clinic a man of eighty-three years was reported with typical mitral rheumatic endocardi-



Fig. 45 (Case IV).—There is a necrotic infarct manifest by deficient staining of nuclei of the glomerulus in the center and of the tubules. The tubules in the center present three, dark-staining, finely granular emboli in the capillary tufts. The infectious process spreads through the interstitial tissue which is densely infiltrated by leukocytes, some of which have already invaded the necrotic tubular epithelium. Many of these leukocytes are undergoing necrosis by pyknosis.

tis with superimposed ulcerative endocarditis, but its appearance in patients over sixty is extremely rare. Roughly, 40 per cent of our patients with endocarditis have mitral valvular endocarditis, 40 per cent mitral and aortic endocarditis, and 10 per cent aortic valvular endocarditis alone. The majority

the aortic valve is 70 mm., and the free margins, particularly the posterior and the left, have been destroyed by extensive ulcerations containing heaped-up, irregular, soft masses of mushy, deep purple-red vegetations. The aortic arch shows focal atherosclerotic thickening of the intima. The pulmonary and tricuspid valves are normal.

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dinary infectious process capable of laying down a growth sufficient to produce loss of tissue substance. In this clinic repeated attention has been called to the frequency of *petechial hemorrhages* of miliary type in the conjunctivae as typical of ulcerative endocarditis. In fact, the pathologic diagnosis is oftentimes suggested by this one finding.

In all forms of endocarditis *emboli* are common. They may be present in the skin as petechiae, under the fingernails, under the toenails, in the retina, in the conjunctivae, in other mucosal tissues, in the brain, in the mesenteric vessels, in the kidney and in the spleen. Whipped off from mural thrombi or from the vegetations on the edges of the valves they may be carried into the lung, or if on the left side into the general circulation. Then one finds the picture of *infarction* complicating the picture of the heart disease. Monoplegia, hemiplegia, loss of vision, cranial nerve palsy, convulsion, pleuritis, pulmonary infarction, mesenteric occlusion, block of the peripheral vessels with gangrene of the extremities, blood in the urine, all these and many more follow in the wake of endocarditis.

The most striking features in examination of many of these patients are *pallor*, *apprehension*, *petechiae*, *murmurs*, *fever*, *loss of weight*, *exhaustion* and *splenic enlargement*. One may not find a murmur and yet have all the other evidences of an infectious endocarditis but sooner or later in our average adult case a murmur will develop.

Differential Diagnosis

It is impossible to more than touch those conditions which must be differentiated from the commonest type of "endocarditis of superimposition"—that is, from subacute bacterial endocarditis. Many diseases come in for consideration. The differential diagnosis in a case of obscure fever requires the use of every known diagnostic procedure if a specific laboratory test is not reported as positive early in the course. With the movement of troops and our civilian population we will have to revise our concepts of what is common to our own communities and be prepared to recognize those diseases which we have ordinarily thought afflicted only our neighbor. In

of subacute cases of ulcerative endocarditis are superimposed on rheumatic pancarditis.

Clinical Discussion

DR. LEROY H. SLOAN: To attempt to cover adequately all of the features which these last two patients suggest would take us far afield. For clinical purposes I shall only touch on certain findings which may be helpful in general practice.

The ordinary endocarditis produced or associated with the "rheumatic ring" is a benign, deforming, obstructive type which for convenience we call "rheumatic endocarditis." The "rheumatic ring" is made up of tonsillitis, rheumatic fever, scarlet fever, pharyngitis, sinusitis and chorea. In this associated benign endocarditis a fibroblastic deformity results. The heart compensates and life continues only to terminate later because of the mechanical difficulties incident to the one or more deformities; or death occurs from intercurrent infection or accident or when there is superimposed upon the already damaged valve a type of lesion which we usually call verrucous implants of subacute bacterial endocarditis. Now, as Dr. Schiller has pointed out, usually this condition occurs in relative youth. However, in Case IV we have a man who at the age of seventy-seven years picks out from all of the possibilities to which the human is exposed an endocarditis with ulceration.

Clinically, in everyday practice one encounters the benign form of endocarditis which we call rheumatic endocarditis and a second form which we term *subacute bacterial endocarditis*. In the latter condition we search through the history for at least one member of the rheumatic ring. We also look for evidence of heart disease, but it is not always prominent. We make frequent blood cultures, using both ordinary and special media. We are looking primarily for *Streptococcus viridans*, but in this clinic Dr. Schiller's predecessor, Dr. Jaffe, reported a subacute bacterial endocarditis due to a pure strain of the influenza bacillus. It is likely that endocarditis due to attenuated forms of other bacteria may give rise to the same picture of long-continued fever.

Ulcerative endocarditis may be associated with any or-

CUMULATIVE INDEX

- ACAROFPHOSIA, *Jan.*, 119
 Acne keloid, radium treatment, *Jan.*, 155
 rosacea, *Jan.*, 173
 vulgaris, *Jan.*, 175
 vitamin D in, *Jan.*, 62
 Acutis, *Jan.*, 79
 Acrodynia, thiamine in, *Jan.*, 54
 Alcohol, subarachnoid injection, deleterious effects, *Jan.*, 255
 Allergic dermatitis, *Jan.*, 14, 153
 Anemia, Cooley's, *Jan.*, 223
 hemolytic, congenital, *Jan.*, 219
 sickle cell, *Jan.*, 224
 Angioma cavernosum, radium treatment, *Jan.*, 134
 Antitoxin, erysipelas, *Jan.*, 90
 Anus, pruritus, *Jan.*, 117
 Aorta, coarctation, symptomless, *Jan.*, 269
 Arsenic in psoriasis, *Jan.*, 190
 Arsenical polyneuritis, pyridoxine in, *Jan.*, 57
 Arthritis, vitamin D in, *Jan.*, 62
 Ascorbic acid in skin diseases, *Jan.*, 58
 Aspiration pneumonia, *Jan.*, 253
 Atopic eczema, *Jan.*, 102

 BARBER'S itch, *Jan.*, 85
 Barbiturates, skin eruption due to, *Jan.*, 145
 Bath, colloid, in lichen urticatus, *Jan.*, 167
 in pruritus, *Jan.*, 116
 Biologic oxidation, vitamins and, *Jan.*, 50
 Biopsy, cervical, *Jan.*, 210
 Bromides, skin eruption due to, *Jan.*, 144
 Brouchitis, acute, in infants and children, *Jan.*, 249
 capillary, *Jan.*, 250
 Bockhart's impetigo, *Jan.*, 87
 Boils, *Jan.*, 91

 Bronchopneumonia in infants and children, *Jan.*, 251

 CALGUM in lichen urticatus, *Jan.*, 165
 Capillary fragility, Rumpel-Leeds test, *Jan.*, 59
 Carbuncle, *Jan.*, 95
 Carcinoma of cervix, *Jan.*, 210
 prophylaxis, *Jan.*, 215
 Cathartics and irritable colon, *Jan.*, 228
 Cement dermatitis, *Jan.*, 26
 Cervix uteri, biopsy, *Jan.*, 210
 carcinoma, *Jan.*, 210
 prophylaxis, *Jan.*, 215
 examination, *Jan.*, 200
 Chancres, *Jan.*, 65
 Children, respiratory tract diseases in, *Jan.*, 237
 skin diseases in, *Jan.*, 163
 Chlorhydroxyquinoline in impetigo contagiosa, *Jan.*, 171
 Christmas tree dermatitis, *Jan.*, 18
 Chrome dermatitis, *Jan.*, 25
 Chrysanthemum dermatitis, *Jan.*, 16
 Chrysarobin in psoriasis, *Jan.*, 189
 Coarctation of aorta, symptomless, *Jan.*, 269
 Cold, common, in infants and children, *Jan.*, 237
 Colloid baths in lichen urticatus, *Jan.*, 167
 in pruritus, *Jan.*, 116
 Colon, irritable, *Jan.*, 227
 Colposcopy in carcinoma of cervix, *Jan.*, 213
 Condyloma acuminata, *Jan.*, 194
 latum, *Jan.*, 68
 Contact dermatitis, *Jan.*, 13, 154
 Cook's emulsion base, *Jan.*, 116
 Cooley's anemia, *Jan.*, 223
 Cough in infants and children, *Jan.*, 241
 Croup, spasmodic, *Jan.*, 248

this connection we must expect more *malaria* in this community, not alone in our addicts to morphine and heroin (as members of our Medical Department have already emphasized) but in returning troops and returning civilians. A recurrent chill, fever, sweat, headache, stomach ache, nausea and vomiting with splenomegaly and a leukopenia will likely give the lead, although in this clinic in the case of at least two patients who died of malignant malaria a high leukocytosis was found—this in “line runners” who contracted malaria by passing an infected needle from addict to addict. (See reports by Feinberg, Eaton and Volini.) Our laboratories must be prepared to conduct tests for the presence of the organisms of typhoid, paratyphoid A and B, undulant fever with its three causative organisms, tularemia, rat-bite fever, Haverhill fever, typhus fever, Rocky Mountain spotted fever, trichiniasis, malaria and amebic and bacillary dysentery. While one may deplore the necessity of numerous laboratory procedures at the expense of sharp clinical examination and observation, a goodly group of patients will not be steered along the proper course without them.

- Impetigo circinata, *Jan.*, 85, 86
 contagiosa, *Jan.*, 84, 168
 treatment, *Jan.*, 86
 Industrial dermatitis, *Jan.*, 21
 Infants, respiratory tract diseases in, *Jan.*, 237
 skin diseases in, *Jan.*, 163
 Inoculation tuberculosis, *Jan.*, 77, 78
 Irritable colon, *Jan.*, 227

 JAUNDICE, hemolytic, congenital, *Jan.*, 220

 KELOID, radium treatment, *Jan.*, 136
 Keratosis, pilaris, vitamin A in, *Jan.*, 52
 senile, radium treatment, *Jan.*, 135

 LARYNGITIS, acute, in infants and children, *Jan.*, 245
 catarrhal, *Jan.*, 248
 Laryngotracheobronchitis, acute, *Jan.*, 246
 Leukemia cutis, *Jan.*, 3, 6
 Leukoplakia, radiotherapy, *Jan.*, 135
 Leukorrhea, etiologic diagnosis, *Jan.*, 202
 treatment, *Jan.*, 208
 Lichen scrofulosorum, *Jan.*, 79
 spinulosis, vitamin A in, *Jan.*, 52
 urticatus, *Jan.*, 163
 Lip, impetigo, *Jan.*, 85
 perlèche, *Jan.*, 172
 Lipiodol, subarachnoid injection, deleterious effects, *Jan.*, 255
 Liver extract in skin diseases, *Jan.*, 57
 Lobar pneumonia. See *Pneumonia*.
 Lotio sulfurata, *Jan.*, 41
 Lupus erythematosus, *Jan.*, 29
 discoïd, chronic, *Jan.*, 29, 40
 in exacerbation, *Jan.*, 32, 44
 disseminate, acute, *Jan.*, 34, 44
 chronic, *Jan.*, 31, 40
 in exacerbation, *Jan.*, 32, 44
 nicotinic acid in, *Jan.*, 56
 vulgaris, *Jan.*, 75
 Lymphoblastoma cutis, *Jan.*, 1
 Lymphogranulomatosis cutis, *Jan.*, 4, 10, 11

 MERCURY in impetigo contagiosa, *Jan.*, 170

 Moniliasis, *Jan.*, 160, 167
 Moniliatin, *Jan.*, 151
 Mucons parches, *Jan.*, 68
 Mycosis fungoides, *Jan.*, 3, 7
 Mycotic vaginitis, *Jan.*, 203, 207, 209

 NAIL polish dermatitis, *Jan.*, 16
 Nails, ringworm, *Jan.*, 160
 Nasal drops, administration to children, *Jan.*, 239-241
 Neurotic excoriations, *Jan.*, 119
 Nervus vasculosus, radium treatment, *Jan.*, 134
 Nicotinic acid in skin diseases, *Jan.*, 55
 Nikolsky sign, *Jan.*, 35
 Nosebleed, *Jan.*, 243

 OFFICE procedures, gynecologic, *Jan.*, 195
 Ointments, vehicles of, *Jan.*, 108
 Onchomycosis, *Jan.*, 160
 Onychia mycosis, *Jan.*, 160

 PAIN, intractable, subarachnoid alcohol injections for, *Jan.*, 264
 Patch test in industrial dermatitis, *Jan.*, 23
 Pellagra, nicotinic acid in, *Jan.*, 56
 Pemphigoid, *Jan.*, 86
 Pemphigus neonatorum, *Jan.*, 86
 vulgaris, vitamin D in, *Jan.*, 63
 Perlèche, *Jan.*, 172
 Phenolphthalein, skin eruption due to, *Jan.*, 143
 Pityriasis rosea, *Jan.*, 182
 rubra pilaris, vitamin A in, *Jan.*, 52
 Plantar warts, *Jan.*, 191, 194
 radium treatment, *Jan.*, 135
 Pneumonia, aspiration, *Jan.*, 253
 lobar, in infants and children, *Jan.*, 250
 pneumatic, *Jan.*, 253
 Polyneuritis, arsenical, pyridoxine in, *Jan.*, 57
 Pylsensitivity, dermatitis due to, *Jan.*, 14, 19
 Primrose dermatitis, *Jan.*, 18
 Pruritus ani, *Jan.*, 117
 essential, *Jan.*, 109
 generalized, *Jan.*, 110
 localized, *Jan.*, 117

- DARIER's disease, vitamin A in, *Jan.*, 53
- Dehydrocholesterol, activated, *Jan.*, 60
- Dermatitis, allergic, *Jan.*, 14
 of hands, *Jan.*, 153
 contact, *Jan.*, 13
 of hands, *Jan.*, 154
 eczematous, *Jan.*, 13
 "emotional," of fingers, *Jan.*, 155
 hair-dye, *Jan.*, 98
 industrial, *Jan.*, 21
 nonsensitization, *Jan.*, 13
 papillaris capillitii, radium treatment, *Jan.*, 135
 seborrheic, *Jan.*, 180
 sensitization, *Jan.*, 13, 14
 supposedly psychogenic, *Jan.*, 101
 venenata, *Jan.*, 13
- Dermatoses, toxic, *Jan.*, 139
- Diathermy, short wave, in carbuncle, *Jan.*, 96
- Dress shield dermatitis, *Jan.*, 17
- Drug eruptions, *Jan.*, 141, 142
 sensitivity, vitamin C in, *Jan.*, 59
- ECTHYMA, *Jan.*, 88
- Eczema ani, *Jan.*, 106
 atopic, *Jan.*, 102
 impetigenized, *Jan.*, 106
 nuchae, *Jan.*, 105
 varicose, with eczematids, *Jan.*, 105
- Eczema-dermatitis, treatment, in adults, *Jan.*, 97
- Eczematoid ringworm, *Jan.*, 107
- Eczematous dermatitis, *Jan.*, 13
- Emotional dermatitis of fingers, *Jan.*, 155
 upsets and irritable colon, *Jan.*, 229
- Endocarditis, vegetative and ulcerative, clinical and pathological conference at Cook County Hospital, *Jan.*, 296
- Enemas and irritable colon, *Jan.*, 228
- Epidermophytosis of feet, *Jan.*, 151
 simulating industrial dermatitis, *Jan.*, 26
- Epistaxis in infants and children, *Jan.*, 243
- Epithelioma, basal cell, radium treatment, *Jan.*, 135
- Erysipelas, *Jan.*, 89
 antitoxin treatment, *Jan.*, 90
 sulfanilamide in, *Jan.*, 91
 ultraviolet light in, *Jan.*, 91
- Erythema group of skin diseases, etiology, *Jan.*, 139
 induratum, *Jan.*, 79
 nodosum, *Jan.*, 147
- Erythematous lupus, *Jan.*, 29
- Examination, gynecologic, *Jan.*, 195
- FEET, ringworm, *Jan.*, 151
- Fever therapy, in syphilis, *Jan.*, 74
- Follicles, *Jan.*, 79
- Fungous infections, superficial, *Jan.*, 151
- Furuncle, *Jan.*, 91
 immunization, *Jan.*, 94
 treatment, *Jan.*, 92
- GOLD salts in lupus erythematosus, *Jan.*, 43, 45
- Gonorrheal vaginitis, *Jan.*, 203
- Gumma, *Jan.*, 70
- Gynecologic examination, *Jan.*, 195
 office procedures, *Jan.*, 195
- HAIR-DYE dermatitis, *Jan.*, 98
- Hands, dermatitis, allergic, simulating ringworm, *Jan.*, 153
 contact, *Jan.*, 154
 ringworm, *Jan.*, 151
 toxic eruption, with ringworm of feet, *Jan.*, 151
- Hemolytic anemia, congenital, *Jan.*, 219
 jaundice, congenital or familial, *Jan.*, 220
- Herpes simplex, *Jan.*, 183
 zoster, *Jan.*, 185
- Hives, *Jan.*, 145
- Hodgkin's disease, clinical and pathological conference at Cook County Hospital, *Jan.*, 283
 cutaneous lesions, *Jan.*, 4, 9
- Hyperkeratosis, follicular, vitamin A in, *Jan.*, 52
 vitamin C in, *Jan.*, 59
- Hyperpyrexia in syphilis, *Jan.*, 74
- ICTERUS. See *Jaundice*.
- Impetigo, Bockhart's, *Jan.*, 87
 bullosa, *Jan.*, 86

- Varicose eczema with eczematids, *Jan.*, 105
Varnish remover dermatitis, *Jan.*, 25
Verruca acuminata, *Jan.*, 191
 vulgaris, *Jan.*, 190
Viosterol, *Jan.*, 60
Vitamin A in skin diseases, *Jan.*, 50
Vitamin B complex in skin diseases, *Jan.*, 54
Vitamin B₆ in skin diseases, *Jan.*, 57
Vitamin C in skin diseases, *Jan.*, 58
Vitamin D in skin diseases, *Jan.*, 60
Vitamin P in skin diseases, *Jan.*, 60
- Vitamins, deficiencies, primary and secondary, *Jan.*, 49
 in dermatology, *Jan.*, 47
Vulva, pruritus, *Jan.*, 118
- WARTS, *Jan.*, 190
 flat, *Jan.*, 191, 194
 plantar, *Jan.*, 191, 194
 radium treatment, *Jan.*, 135
 seborrhoeic, *Jan.*, 191, 193
- YEAST infection of lip, *Jan.*, 172
 of vagina, *Jan.*, 205, 207, 209

- Pruritus of scalp, *Jan.*, 119
 secondary, *Jan.*, 120
 treatment, *Jan.*, 109
 vulvae, *Jan.*, 118
 Psoriasis, *Jan.*, 187
 vitamin D in, *Jan.*, 62
 Purpura, *Jan.*, 146
 Pusey's calamine lotion, *Jan.*, 116
 Pyogenic infections of skin, *Jan.*, 83
 Pyridoxine in skin diseases, *Jan.*, 57
- QUININE in lupus erythematosus, *Jan.*, 42
- RADIUM treatment of skin diseases, *Jan.*, 123, 132
 skin damage from, *Jan.*, 137
 Radon in skin diseases, *Jan.*, 137
 Rheumatic pneumonia, *Jan.*, 253
 Riboflavin in skin diseases, *Jan.*, 55
 Ringworm, eczematoid, *Jan.*, 107
 of hands and feet, *Jan.*, 151
 of nails, *Jan.*, 160
 of scalp, *Jan.*, 161
 treatment and prophylaxis, *Jan.*, 157
 Roentgen burns, vitamin D in, *Jan.*, 63
 treatment of skin diseases, *Jan.*, 123
 skin damage from, *Jan.*, 137
 Roseolar, *Jan.*, 66, 178
 Rumpel-Leeds test for capillary fragility, *Jan.*, 59
- SCALP, pruritus, *Jan.*, 119
 ringworm, *Jan.*, 161
 Scars, hypertrophic, radium treatment, *Jan.*, 136
 Scleroderma, vitamin D in, *Jan.*, 63
 Schiller test, *Jan.*, 213
 Scrofuloderma, *Jan.*, 76
 Seborrheic dermatitis, *Jan.*, 180
 wart, *Jan.*, 191, 193
 Schwartzman phenomenon, *Jan.*, 36
 Sickle cell anemia, *Jan.*, 224
 Silver nitrate in impetigo contagiosa, *Jan.*, 171
 Skin diseases, erythema group, etiology, *Jan.*, 139
 in infants and children, *Jan.*, 163
 miscellaneous, *Jan.*, 175
- Skin diseases, radium treatment, *Jan.*, 123, 132
 roentgen treatment, *Jan.*, 123
 symposium on, *Jan.*, 1
 vitamins in, *Jan.*, 47
 fungous infections, *Jan.*, 151
 leukemic lesions, *Jan.*, 3
 pyogenic infections, *Jan.*, 83
 radiotherapy damage, *Jan.*, 137
 syphilitic lesions, *Jan.*, 65
 tuberculosis, *Jan.*, 74
 Subarachnoid injections of lipiodol and alcohol, deleterious effects, *Jan.*, 255
 Sulfanilamide in erysipelas, *Jan.*, 91
 in lupus erythematosus, *Jan.*, 44
 Sulfathiazole in carbuncle, *Jan.*, 96
 in furuncle, *Jan.*, 94
 in impetigo contagiosa, *Jan.*, 172
 Sulfonamides, skin eruption due to, *Jan.*, 145
 Sulfur in impetigo contagiosa, *Jan.*, 171
 Syphilids, *Jan.*, 66
 Syphilis, cutaneous, *Jan.*, 65
 treatment, *Jan.*, 71
- THIAMINE in skin diseases, *Jan.*, 54
 Thrush, *Jan.*, 160
 Tinea, *Jan.*, 151
 cruris, *Jan.*, 159
 marginatum, *Jan.*, 159
 tonsurans, *Jan.*, 161
 Toxic dermatoses, *Jan.*, 139
 Trichomonas vaginitis, *Jan.*, 203, 205, 208
 Trichophyton, *Jan.*, 151
 Tuberculids, *Jan.*, 79, 147
 Tuberculosis, cutaneous, *Jan.*, 74
 cutis verrucosa, *Jan.*, 77
 inoculation, *Jan.*, 77, 78
- ULTRAVIOLET light in erysipelas, *Jan.*, 91
 in impetigo contagiosa, *Jan.*, 172
 Urticaria, *Jan.*, 145
 papular, of childhood, *Jan.*, 163
- VAGINAL discharges, etiologic diagnosis, *Jan.*, 202
 Vaginitis, gonorrheal, *Jan.*, 203
 mycotic, *Jan.*, 203, 207, 209
 trichomonas, *Jan.*, 203, 205, 208



- Pruritus of scalp, *Jan.*, 119
 secondary, *Jan.*, 120
 treatment, *Jan.*, 109
 vulvae, *Jan.*, 118
 Psoriasis, *Jan.*, 187
 vitamin D in, *Jan.*, 62
 Purpura, *Jan.*, 146
 Pusey's calamine lotion, *Jan.*, 116
 Pyogenic infections of skin, *Jan.*, 83
 Pyridoxine in skin diseases, *Jan.*, 57
- QUININE in lupus erythematosus,
Jan., 42
- RADIUM treatment of skin diseases,
Jan., 123, 132
 skin damage from, *Jan.*, 137
 Radon in skin diseases, *Jan.*, 137
 Rheumatic pneumonia, *Jan.*, 253
 Riboflavin in skin diseases, *Jan.*, 55
 Ringworm, eczematoid, *Jan.*, 107
 of hands and feet, *Jan.*, 151
 of nails, *Jan.*, 160
 of scalp, *Jan.*, 161
 treatment and prophylaxis, *Jan.*,
 157
 Roentgen burns, vitamin D in, *Jan.*,
 63
 treatment of skin diseases, *Jan.*,
 123
 skin damage from, *Jan.*, 137
 Roseolar, *Jan.*, 66, 178
 Rumpel-Leeds test for capillary
 fragility, *Jan.*, 59
- SCALP, pruritus, *Jan.*, 119
 ringworm, *Jan.*, 161
 Scars, hypertrophic, radium treat-
 ment, *Jan.*, 136
 Scleroderma, vitamin D in, *Jan.*, 63
 Schiller test, *Jan.*, 213
 Scrofuloderma, *Jan.*, 76
 Seborrheic dermatitis, *Jan.*, 180
 wart, *Jan.*, 191, 193
 Schwartzman phenomenon, *Jan.*, 36
 Sick cell anemia, *Jan.*, 224
 Silver nitrate in impetigo contagiosa,
Jan., 171
 Skin diseases, erythema group, eti-
 ology, *Jan.*, 139
 in infants and children, *Jan.*,
 163
 miscellaneous, *Jan.*, 175
- Skin diseases, radium treatment, *Jan.*,
 123, 132
 roentgen treatment, *Jan.*, 123
 symposium on, *Jan.*, 1
 vitamins in, *Jan.*, 47
 fungous infections, *Jan.*, 151
 leukemic lesions, *Jan.*, 3
 pyogenic infections, *Jan.*, 83
 radiotherapy damage, *Jan.*, 137
 syphilitic lesions, *Jan.*, 65
 tuberculosis, *Jan.*, 74
 Subarachnoid injections of lipiodol
 and alcohol, deleterious effects,
Jan., 255
 Sulfanilamide in erysipelas, *Jan.*, 91
 in lupus erythematosus, *Jan.*, 44
 Sulfathiazole in carbuncle, *Jan.*, 96
 in furuncle, *Jan.*, 94
 in impetigo contagiosa, *Jan.*, 172
 Sulfonamides, skin eruption due to,
Jan., 145
 Sulfur in impetigo contagiosa, *Jan.*,
 171
 Syphilids, *Jan.*, 66
 Syphilis, cutaneous, *Jan.*, 65
 treatment, *Jan.*, 71
- THIAMINE in skin diseases, *Jan.*, 54
 Thrush, *Jan.*, 160
 Tinea, *Jan.*, 151
 cruris, *Jan.*, 159
 marginatum, *Jan.*, 159
 tonsurans, *Jan.*, 161
 Toxic dermatoses, *Jan.*, 139
 Trichomonas vaginitis, *Jan.*, 203,
 205, 208
 Trichophyton, *Jan.*, 151
 Tuberculids, *Jan.*, 79, 147
 Tuberculosis, cutaneous, *Jan.*, 74
 cutis verrucosa, *Jan.*, 77
 inoculation, *Jan.*, 77, 78
- ULTRAVIOLET light in erysipelas, *Jan.*,
 91
 in impetigo contagiosa, *Jan.*, 172
 Urticaria, *Jan.*, 145
 papular, of childhood, *Jan.*, 163
- VAGINAL discharges, etiologic diag-
 nosis, *Jan.*, 202
 Vaginitis, gonorrheal, *Jan.*, 203
 mycotic, *Jan.*, 203, 207, 209
 trichomonas, *Jan.*, 203, 205, 208

- Varicose eczema with eczematids, *Jan.*, 105
Varnish remover dermatitis, *Jan.*, 25
Verruca acuminata, *Jan.*, 191
 vulgaris, *Jan.*, 190
Viosterol, *Jan.*, 60
Vitamin A in skin diseases, *Jan.*, 50
Vitamin B complex in skin diseases, *Jan.*, 54
Vitamin B₆ in skin diseases, *Jan.*, 57
Vitamin C in skin diseases, *Jan.*, 58
Vitamin D in skin diseases, *Jan.*, 60
Vitamin P in skin diseases, *Jan.*, 60
- Vitamins, deficiencies, primary and secondary, *Jan.*, 49
 in dermatology, *Jan.*, 47
Vulva, pruritus, *Jan.*, 118
- WARTS, *Jan.*, 190
 flat, *Jan.*, 191, 194
 plantar, *Jan.*, 191, 194
 radium treatment, *Jan.*, 135
 seborrheic, *Jan.*, 191, 193
- YEAST infection of lip, *Jan.*, 172
 of vagina, *Jan.*, 203, 207, 209